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=> d ide can 14

L4   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   161384-17-4  REGISTRY
CN   Proteinase, matrix metallo-, MT-MMP-1 (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Matrix metalloprotease 14
CN   Matrix metalloproteinase 14
CN   Matrix metalloproteinase MT 1
CN   Matrix metalloproteinase MT-MMP-1
CN   Matrix metalloproteinase MT1-MMP
CN   Membrane type 1 matrix metalloproteinase
CN   Membrane type-1 matrix metalloprotease
CN   Membrane-type matrix metalloprotease 1
CN   Membrane-type matrix metalloproteinase 1
CN   Membrane-type matrix metalloproteinase MT1-MMP
CN   Membrane-type metalloproteinase MT1-MMP
CN   MMP-14
CN   MT-MMP1
CN   MT1-MMP
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   AGRICOLA, BIOSIS, CA, CAPLUS, CIN, TOXCENTER, USPAT2,
       USPATFULL
DT.CA  CAplus document type:  Conference; Dissertation; Journal; Patent
RL.P   Roles from patents:  ANST (Analytical study); BIOL (Biological study);
       MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC
       (Process); PRP (Properties); USES (Uses)
RLD.P  Roles for non-specific derivatives from patents:  BIOL (Biological
       study); USES (Uses)
RL.NP  Roles from non-patents:  ANST (Analytical study); BIOL (Biological
       study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP
       (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents:  BIOL (Biological
       study); PROC (Process); PRP (Properties)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
             942 REFERENCES IN FILE CA (1907 TO DATE)
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6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
951 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:389458

REFERENCE 2: 140:389388

REFERENCE 3: 140:389365

REFERENCE 4: 140:389134

REFERENCE 5: 140:386423

REFERENCE 6: 140:385874

REFERENCE 7: 140:373167

REFERENCE 8: 140:372965

REFERENCE 9: 140:372236

REFERENCE 10: 140:370800

=> fil hcaplus
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FILE COVERS 1907 - 8 Jun 2004 VOL 140 ISS 24
FILE LAST UPDATED: 7 Jun 2004 (20040607/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all hitstr tot l53

L53 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:864165 HCAPLUS
DN 140:57378
ED Entered STN: 05 Nov 2003
TI **Membrane type-1 matrix metalloproteinase** (**MT1-MMP**) processing of pro-α v **integrin** regulates cross-talk between . **alpha.**vβ3 and α 2β1 **integrins** in breast carcinoma cells
AU **Baciu, Peter C.**; Suleiman, E. Aisha; Deryugina, Elena I.; Strongin, Alex Y.
CS **Allergan** Inc., Irvine, CA, 2525, USA
SO Experimental Cell Research (2003), 291(1), 167-175

CODEN: ECREAL; ISSN: 0014-4827
PB Elsevier Science
DT Journal
LA English
CC 14-1 (Mammalian Pathological Biochemistry)
AB We have recently demonstrated that in breast carcinoma MCF7 cells **MT1-MMP** processes the α v, **.alpha** .3, and α 5 **integrin** precursors generating the resp. mature S-S-linked heavy and light α -chains. The precursor of α 2 **integrin subunit** was found resistant to **MT1-MMP** proteolysis. The processing of the α v **subunit** by **MT1-MMP** facilitated α vβ3-dependent adhesion, activation of FAK signaling pathway, and migration of MCF7 cells on vitronectin. To elucidate further the effects of **MT1-MMP** on cellular **integrins**, we examined the functional activity of α 5β1 and α 2β1 **integrins** in MCF7 cells expressing **MT1-MMP.** Either expression of **MT1-MMP** alone or its coexpression with α vβ3 failed to affect the functionality of . **alpha.**5β1 **integrin**, and adhesion of cells to fibronectin. **MT1-MMP**, however, profoundly affected the cross-talk involving α vβ3 and **.alpha** .2β1 **integrins.** In **MT1-MMP**-deficient cells, **integrin** α vβ3 suppressed the functional activity of the collagen-binding α 2β1 **integrin** receptor and diminished cell adhesion to type I collagen. Co-expression of **MT1-MMP** with **integrin** . **alpha.**vβ3 restored the functionality of **.alpha** .2β1 **integrin** and, consequently, the ability of MCF7 cells to adhere efficiently to collagen. We conclude that the **MT1-MMP**-controlled cross-talk between α vβ3 and . **alpha.**2β1 **integrins** supports binding of aggressive, **MT1-MMP**-, and α vβ3 **integrin** -expressing malignant cells on type I collagen, the most common substratum of the extracellular **matrix.**
ST MTMMP **integrin** cell adhesion migration breast carcinoma
IT Adhesion, biological
Cell proliferation
Extracellular **matrix**
Human
(**MT1-MMP** processing of pro-α v **integrin** regulated cross-talk between α vβ3 and α 2β1 **integrins**, cell adhesion to collagen and migration in human breast carcinoma)
IT Mammary gland, neoplasm
(carcinoma; **MT1-MMP** processing of pro-α v **integrin** regulated cross-talk between α vβ3 and α 2β1 **integrins** , cell adhesion to collagen and migration in human breast carcinoma)
IT Cell migration
(invasion; **MT1-MMP** processing of pro-α v **integrin** regulated cross-talk between α vβ3 and α 2β1 **integrins** , cell adhesion to collagen and migration in human breast carcinoma)
IT Collagens, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type I; **MT1-MMP** processing of pro-α v **integrin** regulated cross-talk between α vβ3 and α 2β1 **integrins**, cell adhesion to collagen and migration in human breast carcinoma)
IT **Integrins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(α **v**, pro-; **MT1-MMP**
processing of pro-α **v integrin**
regulated cross-talk between α **v**.beta.3 and
α 2β1 **integrins**, cell adhesion to collagen
and migration in human breast carcinoma)

IT **Integrins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α **v**.beta.3; **MT1-MMP**
processing of pro-α **v integrin**
regulated cross-talk between α **v**.beta.3 and
α 2β1 **integrins**, cell adhesion to collagen
and migration in human breast carcinoma)

IT **Integrins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α 2β1; **MT1-MMP** processing of
pro-α **v integrin** regulated
cross-talk between α **v**.beta.3 and
α 2β1 **integrins**, cell adhesion to collagen
and migration in human breast carcinoma)

IT **Integrins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α **5**.beta.1; **MT1-MMP**
processing of pro-α **v integrin**
regulated cross-talk between α **v**.beta.3 and
α 2β1 **integrins**, cell adhesion to collagen
and migration in human breast carcinoma)

IT **161384-17-4**, **Membrane type-1**
matrix metalloproteinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**MT1-MMP** processing of pro-α v
integrin regulated cross-talk between α vβ3
and α 2β1 **integrins**, cell adhesion to
collagen and migration in human breast carcinoma)

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD

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IT **161384-17-4**, **Membrane type-1**
matrix metalloproteinase

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**MT1-MMP** processing of pro-α v
integrin regulated cross-talk between α vβ3
and α 2β1 **integrins**, cell adhesion to
collagen and migration in human breast carcinoma)
RN 161384-17-4 HCAPLUS
CN Proteinase, matrix metallo-, MT-MMP-1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L53 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2002:793746** HCAPLUS
DN **137:273251**
ED Entered STN: 18 Oct 2002
TI Methods of **screening** and using inhibitors of
angiogenesis
IN **Baciu, Peter C.; Zhang, Heying; Manuel, Verna M.**
PA **Allergan**, Inc., USA
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N
CC 1-12 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002081627	A2	20021017	WO 2002-US10501	20020403 <--
	WO 2002081627	A3	20031218		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003171271	A1	20030911	US 2002-115718	20020403 <--
	EP 1393075	A2	20040303	EP 2002-763922	20020403 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	US 2001-281512P	P	20010404 <--		
	WO 2002-US10501	W	20020403 <--		

AB A method of **screening** for agents which are able to inhibit **angiogenesis.** Such agent have therapeutic application in the treatment of conditions including cancer, macular degeneration and retinopathies. Also included are methods of treating a patient having a pathol. condition characterized by an increase in **angiogenesis** which comprises administering to the patient an agent capable of inhibiting activation of an **integrin subunit.**
ST drug **screening angiogenesis** inhibitor **integrin matrix metalloproteinase** eye neovascularization
IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PECAM-1; methods of **screening** and using inhibitors of **angiogenesis**)
IT Gene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(expression; methods of **screening** and using inhibitors of **angiogenesis**)
IT **Angiogenesis**

Angiogenesis inhibitors
Chromatography
Drug screening
Electrophoresis
Human
(methods of **screening** and using inhibitors of **angiogenesis**)

IT Reporter gene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(methods of **screening** and using inhibitors of **angiogenesis**)

IT **Eye, disease**
(**neovascularization**, cornea; methods of **screening** and using inhibitors of **angiogenesis**)

IT **Angiogenesis**
(neovascularization, eye, cornea; methods of **screening** and using inhibitors of **angiogenesis**)

IT **Integrins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α **subunit**; methods of **screening** and using inhibitors of **angiogenesis**)

IT 146480-35-5, **Matrix metalloproteinase** 2 152787-66-1, Pro **MMP**-9 **161384-17-4**, **Matrix metalloproteinase MT1-MMP**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(methods of **screening** and using inhibitors of **angiogenesis**)

IT **161384-17-4**, **Matrix metalloproteinase MT1-MMP**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(methods of **screening** and using inhibitors of **angiogenesis**)

RN 161384-17-4 HCAPLUS
CN Proteinase, matrix metallo-, MT-MMP-1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L53 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:209623 HCAPLUS
DN 136:367452
ED Entered STN: 20 Mar 2002
TI An alternative processing of **integrin** α v **subunit** in tumor cells by **membrane type-1 matrix metalloproteinase**
AU Ratnikov, Boris I.; Rozanov, Dmitri V.; Postnova, Tanya I.; **Baciu, Peter G.**; **Zhang, Heying**; DiScipio, Richard G.; Chestukhina, Galina G.; Smith, Jeffrey W.; Deryugina, Elena I.; Strongin, Alex Y.
CS Burnham Institute, La Jolla, CA, 92037, USA
SO Journal of Biological Chemistry (2002), 277(9), 7377-7385
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 14-1 (Mammalian Pathological Biochemistry)
AB **Membrane type-1 matrix metalloproteinase** (**MT1-MMP**) and **.alpha**.vβ3 **integrin** are both essential to cell invasion. Maturation of **integrin** pro-α v chain (pro-.**alpha.**v) involves its **cleavage** by proprotein convertases (PC) to form the disulfide-bonded 125-kDa heavy and 25-kDa light .**alpha.** chains. Our report presents evidence of an alternative pathway of pro-α v processing involving **MT1-MMP**. In breast carcinoma MCF7 cells deficient in **MT1-**

MMP, pro-α v is processed by a conventional furin-like PC, and the mature α v **integrin subunit** is represented by the 125-kDa heavy chain and the 25-kDa light chain commencing from the N-terminal Asp891. In contrast, in cells co-expressing α vβ3 and **MT1-MMP**, **MT1-MMP** functions as an **integrin** convertase. **MT1-MMP** specifically **cleaves** pro-. **alpha.**v, generating a 115-kDa heavy chain with the truncated C terminus and a 25-kDa light chain commencing from the N-terminal Leu892. PC-**cleavable** α 3 and α 5 but not the PC-resistant α 2 **integrin subunit** are also susceptible to **MT1-MMP cleavage.** These novel mechanisms involved in the processing of **integrin . alpha. subunits** underscore the significance and complexity of interactions between **MT1-MMP** and adhesion receptors and suggest that regulation of **integrin** functionality may be an important role of **MT1-MMP** in migrating tumor cells.

ST **integrin alphav MT1 MMP** cancer

IT Neoplasm
(alternative processing of **integrin** α v **subunit** in tumor cells by **membrane type-1 matrix metalloproteinase**)

IT Mammary gland, neoplasm
(carcinoma; alternative processing of **integrin** α v **subunit** in tumor cells by **membrane type-1 matrix metalloproteinase**)

IT **Integrins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α **v**; alternative processing of **integrin** α **v subunit** in tumor cells by **membrane type-1 matrix metalloproteinase**)

IT **Integrins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α **v**.beta.3; alternative processing of **integrin** α **v subunit** in tumor cells by **membrane type-1 matrix metalloproteinase**)

IT **Integrins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α 3; alternative processing of **integrin subunits** in tumor cells by **membrane type-1 matrix metalloproteinase**)

IT **Integrins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α **5**; alternative processing of **integrin subunits** in tumor cells by **membrane type-1 matrix metalloproteinase**)

IT **161384-17-4, Proteinase, matrix metallo-, MT-MMP-1**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(alternative processing of **integrin** α v **subunit** in tumor cells by **membrane type-1 matrix metalloproteinase**)

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD

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IT **161384-17-4**, **Proteinase, matrix metallo-, MT-MMP-1**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(alternative processing of **integrin** α v **subunit** in tumor cells by **membrane type-1 matrix metalloproteinase**)

RN 161384-17-4 HCAPLUS
CN Proteinase, matrix metallo-, MT-MMP-1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> d all hitstr tot l54

L54 ANSWER 1 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2002:90098** HCAPLUS
DN **136:129047**
ED Entered STN: 01 Feb 2002
TI **Screening** methods based on superactivated **.alpha** .vβ3 **integrin**
IN Strongin, Alex Y.; Deryugina, Elena I.
PA The Burnham Institute, USA
SO PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DT Patent
LA English

IC ICM C07K014-47
CC 1-6 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002008280	A2	20020131	WO 2001-US23514	20010726 <--
	WO 2002008280	A3	20030116		
	WO 2002008280	B1	20030320		

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	US 2002025510	A1	20020228	US 2001-916658	20010726 <--
PRAI	US 2000-220706P	P	20000726 <--		

AB The present invention is directed to a method of identifying an inhibitor or enhancer of α vβ3 activity by contacting superactivated α vβ3 **integrin** with one or more mols.; and assaying an α vβ3 **integrin** activity, where reduced α vβ3 identifies an inhibitor of α vβ3 activity and where enhanced **.alpha** .vβ3 activity identifies an enhancer of α vβ3 activity. In a preferred embodiment, a cell, such as a MCF-7 breast carcinoma cell, is transfected with a nucleic acid mol. encoding a superactivated β3 variant, which can have, for example, substantially the amino acid sequence of SEQ ID NO: 6 shown in Figure 3 of the patent.

ST antitumor drug **screening** superactivated **alphav** beta3 **integrin** sequence

IT Animal cell line
(MCF-7; antitumor drug **screening** methods based on superactivated α vβ3 **integrin**)

IT Adhesion, biological
Antitumor agents
Drug screening
Gene therapy
Human
Molecular **cloning**
Neoplasm
Protein sequences
Regeneration, animal
Transformation, genetic
cDNA sequences
(antitumor drug **screening** methods based on superactivated α vβ3 **integrin**)

IT Vitronectin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(binding of; antitumor drug **screening** methods based on superactivated α vβ3 **integrin**)

IT Mammary gland, neoplasm
(carcinoma, MCF-7; antitumor drug **screening** methods based on superactivated α vβ3 **integrin**)

IT Mammary gland
(carcinoma, inhibitors; antitumor drug **screening** methods based on superactivated α vβ3 **integrin**)

IT Transformation, neoplastic
(immortalization; antitumor drug **screening** methods based on superactivated α vβ3 **integrin**)

IT Antibodies

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**integrin** α vβ3-specific; antitumor drug **screening** methods based on superactivated α vβ3 **integrin**)

IT Antitumor agents
(mammary gland carcinoma; antitumor drug **screening** methods based on superactivated α vβ3 **integrin**)

IT **Integrins**
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α **v**.beta.3, enhancers and inhibitors; antitumor drug **screening** methods based on superactivated α **v**.beta.3 **integrin**)

IT 391979-97-8 391979-98-9 391980-01-1
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; antitumor drug **screening** methods based on superactivated α vβ3 **integrin**)

IT **161384-17-4**, **Mt1-mmp**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene encoding; antitumor drug **screening** methods based on superactivated α vβ3 **integrin**)

IT 391979-96-7, DNA (human **integrin** β3- **subunit** cDNA)
391979-99-0 391980-00-0
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; antitumor drug **screening** methods based on superactivated α vβ3 **integrin**)

IT 391980-06-6 391980-07-7
RL: PRP (Properties)
(unclaimed nucleotide sequence; **screening** methods based on superactivated α vβ3 **integrin**)

IT 391980-03-3 391980-04-4 391980-05-5
RL: PRP (Properties)
(unclaimed protein sequence; **screening** methods based on superactivated α vβ3 **integrin**)

IT 116273-52-0
RL: PRP (Properties)
(unclaimed sequence; **screening** methods based on superactivated α vβ3 **integrin**)

IT **161384-17-4**, **Mt1-mmp**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene encoding; antitumor drug **screening** methods based on superactivated α vβ3 **integrin**)

RN 161384-17-4 HCAPLUS
CN Proteinase, matrix metallo-, MT-MMP-1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L54 ANSWER 2 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2001:471280** HCAPLUS
DN **135:193350**
ED Entered STN: 29 Jun 2001
TI Effects of **matrix** proteins on the expression of **matrix metalloproteinase**-2, -9, and -**14** and tissue inhibitors of **metalloproteinases** in human cytotrophoblast cells during the first trimester
AU Xu, Ping; Wang, Yan-Ling; Piao, Yun-Shang; Bai, Su-Xia; Xiao, Zhi-Jie; Jia, Ya-Li; Luo, Shu-Yi; Zhuang, Lin-Zhi
CS State Key Laboratory of Reproductive Biology, Institute of Zoology, Chinese Academy of Sciences, Beijing, 100080, Peop. Rep. China

SO Biology of Reproduction (**2001**), 65(1), 240-246
CODEN: BIREBV; ISSN: 0006-3363
PB Society for the Study of Reproduction
DT Journal
LA English
CC 13-6 (Mammalian Biochemistry)

AB The activity of **matrix metalloproteinases** (**MMPs**) specifies the ability of the trophoblast cell to degrade extracellular **matrix** (ECM) substrates. Usually the process of normal human placentation involves a coordinated interaction between the fetal-derived trophoblast cells and their microenvironment in the uterus. In this study, the effects of ECM proteins on the expression of **MMP**-2, -9, and -**14** (membrane-type **MMP**-1); and the production of tissue inhibitors of **metalloproteinase** (TIMP) type -1, -2, and -3 have been investigated. Cytotrophoblast cells at 9 or 10 wk of gestation were cultured on various ECM coated dishes under serum-free conditions. Gelatin zymog. anal. showed that cells grown on fibronectin (FN), laminin (LN), and vitronectin (VN) secreted more **MMP**-9 (about 1.5- to 3-fold more) than cells cultured on collagen I (Col I), whereas the secretion of **MMP**-9 by cells cultured on collagen IV (Col IV) was only half that by the cells on Col I. Northern Blot anal. gave the same results as zymog., indicating that expression of the **MMP**-9 gene in cytotrophoblast cells can be affected by **matrix** proteins. There was no significant difference in the expression of **MMP**-2 either at protein or mRNA levels among the cells cultured on the different **matrix** substrates. The expression of **MMP**-**14** was regulated in a manner similar to that of **MMP**-2. Using ELISA, we detected higher levels of TIMP-1 in the culture medium of cells grown on VN, LN, and FN compared with that grown on Col I. But the expression of TIMP-3 mRNA was remarkably inhibited by VN, and ECM proteins had no effect on TIMP-1 and TIMP-2 mRNA expression. It was also observed that cultured cytotrophoblast cells expressed the corresponding receptors for the tested **matrix** proteins, such as **integrins** α 1, **.alpha** .5, α 6, β1, and β4. Furthermore, the adhesiveness of cytotrophoblast cells on Col I, Col IV, FN, and LN was increased by 62%, 45%, 21%, and 22%, resp., when compared with adhesiveness on VN. Isolated cytotrophoblast cells remained stationary when cultured on dishes coated with Col I and Col IV, but they assumed a more motile morphol. and aggregated into a network when cultured on LN and VN. These data indicate that human trophoblast cells interact with their microenvironment to control their behavior and function.

ST extracellular **matrix** protein **metalloproteinase** TIMP expression cytotrophoblast placenta pregnancy

IT Trophoblast
(cytotrophoblast; effects of **matrix** proteins on expression of **matrix metalloproteinases** and tissue inhibitors of **metalloproteinases** in human cytotrophoblast during first trimester)

IT Cell adhesion
Extracellular **matrix**
Placenta
(effects of **matrix** proteins on expression of **matrix metalloproteinases** and tissue inhibitors of **metalloproteinases** in human cytotrophoblast during first trimester)

IT Fibronectins
Laminins
Vitronectin
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(effects of **matrix** proteins on expression of **matrix**

metalloproteinases and tissue inhibitors of **metalloproteinases** in human cytotrophoblast during first trimester)

IT **Integrins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(effects of **matrix** proteins on expression of **matrix metalloproteinases** and tissue inhibitors of **metalloproteinases** in human cytotrophoblast during first trimester)

IT Pregnancy
(first trimester; effects of **matrix** proteins on expression of **matrix metalloproteinases** and tissue inhibitors of **metalloproteinases** in human cytotrophoblast during first trimester)

IT Collagens, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(type I; effects of **matrix** proteins on expression of **matrix metalloproteinases** and tissue inhibitors of **metalloproteinases** in human cytotrophoblast during first trimester)

IT Collagens, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(type IV; effects of **matrix** proteins on expression of **matrix metalloproteinases** and tissue inhibitors of **metalloproteinases** in human cytotrophoblast during first trimester)

IT 124861-55-8, TIMP-2 140208-24-8, TIMP-1 145809-21-8, TIMP-3 146480-35-5, **Matrix metalloproteinase**-2 146480-36-6, **Matrix metalloproteinase**-9 **161384-17-4**, **Matrix metalloproteinase-14**
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PROC (Process)
(effects of **matrix** proteins on expression of **matrix metalloproteinases** and tissue inhibitors of **metalloproteinases** in human cytotrophoblast during first trimester)

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IT **161384-17-4**, **Matrix metalloproteinase-14**
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PROC (Process)
(effects of **matrix** proteins on expression of **matrix metalloproteinases** and tissue inhibitors of **metalloproteinases** in human cytotrophoblast during first trimester)

RN 161384-17-4 HCAPLUS
CN Proteinase, matrix metallo-, MT-MMP-1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L54 ANSWER 3 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2001:350147** HCAPLUS
DN **135:316620**
ED Entered STN: 16 May 2001
TI Human hepatocellular carcinoma (HCC) cells require both **.alpha** .3β1 **integrin** and **matrix metalloproteinases** activity for migration and invasion
AU Giannelli, Gianluigi; Bergamini, Carlo; Fransvea, Emilia; Marinosci, Felice; Quaranta, Vito; Antonaci, Salvatore
CS Department of Internal Medicine, Immunology, and Infectious Diseases, University of Bari Medical School, Bari, 70124, Italy
SO Laboratory Investigation (**2001**), 81(4), 613-627
CODEN: LAINAW; ISSN: 0023-6837
PB Lippincott Williams & Wilkins
DT Journal
LA English
CC 14-1 (Mammalian Pathological Biochemistry)
AB Hepatocellular carcinoma (HCC) is the most frequent malignant tumor of the liver; prognosis depends on the tendency to metastasize. Cancer cell invasion is regulated by proteolytic remodeling of extracellular

matrix components and by **integrin** expression. We have shown that **matrix metalloproteinase**-2 (**MMP**-2) and **membrane-type-1 matrix metalloproteinase** (**MT1-MMP**) **cleave** Laminin-5 (Ln-5), stimulating cell migration. Here the authors report that all HCC cells express **MT1-MMP**, migrate on Ln-1 and collagen IV, whereas only HCC cells that express **.alpha**.3β1 **integrin** secrete detectable levels of gelatinases, migrate on Ln-5, and invade through a reconstituted basement membrane (BM). Migration on Ln-5 is blocked by BB-94, an **MMP** inhibitor, and by MIG1, a **monoclonal** antibody that hinders migration on **MMP**-2-**cleaved** Ln-5. Invasion through a reconstituted BM is also inhibited by BB-94. HCC α 3β1-neg. cells migrate on Ln-1 and Collagen IV, but not on Ln-5, and do not invade through a reconstituted BM, although they express **MT1-MMP**. Anti-α 3β1 blocking antibodies inhibit gelatinase activation, cell motility, and cell invasion through Matrigel. In vivo, α 3β1 **integrin** and Ln-5 are expressed in HCC tissue but not in normal liver. In conclusion,these data suggest that both α 3β1 **integrin** and gelatinase activity are required for HCC migration and invasion.

ST alpha3beta1 **integrin** gelatinase hepatocellular carcinoma migration invasion; MMP2 MT1MMP **integrin** hepatocellular carcinoma migration invasion; laminin **integrin** gelatinase hepatocellular carcinoma migration invasion; collagen **integrin** gelatinase hepatocellular carcinoma migration invasion

IT Laminins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(1; **MT1-MMP** of human hepatocellular carcinoma cells migrate on Ln-1 and collagen IV)

IT Laminins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(5; α 3β1 **integrin** of human hepatocellular carcinoma cells migrate on Ln-5 and invade through a reconstituted basement membrane)

IT Liver, neoplasm
(hepatoma; human hepatocellular carcinoma cells require α 3β1 **integrin** and **matrix metalloproteinases** activity for migration and invasion)

IT Cell migration
(human hepatocellular carcinoma cells require α 3β1 **integrin** and **matrix metalloproteinases** activity for migration and invasion)

IT Collagens, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(type IV; **MT1-MMP** of human hepatocellular carcinoma cells migrate on Ln-1 and collagen IV)

IT Basement membrane
(α 3β1 **integrin** of human hepatocellular carcinoma cells migrate on Ln-5 and invade through a reconstituted basement membrane)

IT **Integrins**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(α 3β1; **MT1-MMP** of human hepatocellular carcinoma cells migrate on Ln-5 and collagen IV)

IT 146480-35-5, **MMP** 2
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL

(Biological study)
(**MMP**-2 of human hepatocellular carcinoma cells **cleaved** laminin 5)

IT **161384-17-4, MT1-MMP**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**MT1-MMP** of human hepatocellular carcinoma cells migrate on Ln-1 and collagen IV)

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD

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IT **161384-17-4, MT1-MMP**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**MT1-MMP** of human hepatocellular carcinoma cells migrate on Ln-1 and collagen IV)

RN 161384-17-4 HCAPLUS
CN Proteinase, matrix metallo-, MT-MMP-1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L54 ANSWER 4 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2001:148909** HCAPLUS
DN **134:308361**
ED Entered STN: 01 Mar 2001
TI Collagen-induced proMMP-2 activation by **MT1-MMP** in human dermal fibroblasts and the possible role of **.alpha** .2β1 **integrins**
AU Zigrino, Paola; Drescher, Claudia; Mauch, Cornelia
CS Department of Dermatology, University of Cologne, Cologne, D-50924, Germany
SO European Journal of Cell Biology (**2001**), 80(1), 68-77
CODEN: EJCBDN; ISSN: 0171-9335
PB Urban & Fischer Verlag
DT Journal
LA English
CC 13-2 (Mammalian Biochemistry)
AB Culture of human dermal fibroblasts within a three-dimensional

matrix composed of native type I collagen fibrils is widely used to study the cellular responses to the extracellular **matrix.** Upon contact with native type I collagen fibrils human skin fibroblasts activate latent 72-kDa type IV collagenase/gelatinase (**MMP**-2) to its active 59- and 62-kDa forms. This activation did not occur when cells were cultured on plastic dishes coated with monomeric type I collagen or its denatured form, gelatin. Activation could be inhibited by antibodies against **MT1-MMP**, by the addition of TIMP-2 and by prevention of **MT1-MMP** processing. **MT1-MMP** protein was detected at low levels as active protein in fibroblasts cultured as monolayers. In collagen gel cultures, an increase of the active, 60-kDa **MT1-MMP** and an addnl. 63-kDa protein corresponding to inactive **MT1-MMP** was detected. Incubation of medium containing latent **MMP**-2 with cell membranes isolated from fibroblasts grown in collagen gels caused activation of the enzyme. Furthermore, regulation of **MT1-MMP** expression in collagen cultures seems to be mediated by . **alpha.**2β1 **integrins.** These studies suggest that activation of the proMMP-2 is regulated at the cell surface by a mechanism which is sensitive to cell culture in contact with physiol. relevant **matrixes** and which depends on the ratio of proenzyme and the specific inhibitor TIMP-2.

ST collagen fibril proMMP2 processing gelatinase MT1MMP **integrin** fibroblast

IT Fibroblast
Post-translational processing
(collagen-induced proMMP-2 activation by **MT1-MMP** in human dermal fibroblasts and possible role of α 2β1 **integrins**)

IT Organelle
(fibril; collagen-induced proMMP-2 activation by **MT1-MMP** in human dermal fibroblasts and possible role of α 2β1 **integrins**)

IT Collagens, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(type I, fibril-forming; collagen-induced proMMP-2 activation by **MT1-MMP** in human dermal fibroblasts and possible role of α 2β1 **integrins**)

IT **Integrins**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(α 2β1; collagen-induced proMMP-2 activation by **MT1-MMP** in human dermal fibroblasts and possible role of α 2β1 **integrins**)

IT **161384-17-4, MT1-MMP**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(collagen-induced proMMP-2 activation by **MT1-MMP** in human dermal fibroblasts and possible role of α 2β1 **integrins**)

IT 146480-35-5, **Matrix metalloproteinase** 2
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(collagen-induced proMMP-2 activation by **MT1-MMP** in human dermal fibroblasts and possible role of α 2β1 **integrins**)

IT 148969-98-6, Pro-**matrix metalloproteinase** 2
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(collagen-induced proMMP-2 activation by **MT1-MMP** in human dermal fibroblasts and possible role of α 2β1 **integrins**)

IT 124861-55-8, TIMP-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(collagen-induced proMMP-2 activation by **MT1-MMP** in human dermal fibroblasts and possible role of α 2β1 **integrins** in relation to)

RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD

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IT **161384-17-4, MT1-MMP**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological

occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(collagen-induced proMMP-2 activation by **MT1-MMP** in human dermal fibroblasts and possible role of α 2β1 **integrins**)
RN 161384-17-4 HCAPLUS
CN Proteinase, matrix metallo-, MT-MMP-1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L54 ANSWER 5 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2001:75036** HCAPLUS
DN **134:324375**
ED Entered STN: 01 Feb 2001
TI **MT1-MMP** Initiates Activation of pro-**MMP**-2 and **Integrin** α vβ3 Promotes Maturation of **MMP**-2 in Breast Carcinoma Cells
AU Deryugina, Elena I.; Ratnikov, Boris; Monosov, Edward; Postnova, Tanya I.; DiScipio, Richard; Smith, Jeffrey W.; Strongin, Alex Y.
CS The Burnham Institute, La Jolla, CA, 92037, USA
SO Experimental Cell Research (**2001**), 263(2), 209-223
CODEN: ECREAL; ISSN: 0014-4827
PB Academic Press
DT Journal
LA English
CC 14-1 (Mammalian Pathological Biochemistry)
AB We evaluated cellular mechanisms involved in the activation pathway of **matrix prometalloproteinase**-2 (pro-**MMP**-2), an enzyme implicated in the malignant progression of many tumor types. **Membrane type-1 matrix metalloproteinase** (**MT1-MMP**) **cleaves** the N-terminal prodomain of pro-**MMP**-2 thus generating the activation intermediate that then matures into the fully active enzyme of **MMP**-2. Our results provide evidence on how a collaboration between **MT1-MMP** and **integrin .alpha** .vβ3 promotes more efficient activation and specific, transient docking of the activation intermediate and, further, the mature, active enzyme of **MMP**-2 at discrete regions of cells. We show that coexpression of **MT1-MMP** and **integrin .alpha.**vβ3 in MCF7 breast carcinoma cells specifically enhances in trans autocatalytic maturation of **MMP**-2. The association of **MMP**-2's C-terminal hemopexin-like domain with those mols. of **integrin** α vβ3 which are proximal to **MT1-MMP** facilitates **MMP**-2 maturation. Vitronectin, a specific ligand of **integrin .alpha** .vβ3, competitively blocked the **integrin**-dependent maturation of **MMP**-2. Immunofluorescence and immunopptn. studies supported clustering of **MT1-MMP** and **integrin** α vβ3 at discrete regions of the cell surface. Evidently, the identified mechanisms appear to be instrumental to clustering active **MMP**-2 directly at the invadopodia and invasive front of α vβ3-expressing cells or in their close vicinity, thereby accelerating tumor cell locomotion. (c) 2001 Academic Press.
ST MT1MMP proMMP2 **matrix metalloproteinase** **integrin** breast carcinoma motility
IT Cell membrane
Cell migration
(**MT1-MMP** initiates activation of pro-**MMP**-2 and **integrin** α vβ3 promotes maturation of **MMP**-2 in human breast carcinoma cells in relation to motility)
IT Vitronectin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**MT1-MMP** initiates activation of pro-**MMP**-2 and **integrin** α vβ3 promotes maturation of **MMP**-2 in human breast carcinoma cells in relation to motility)

IT Mammary gland
(carcinoma; **MT1-MMP** initiates activation of pro-**MMP**-2 and **integrin** α vβ3 promotes maturation of **MMP**-2 in human breast carcinoma cells in relation to motility)

IT Sarcoma
(fibrosarcoma; **MT1-MMP** initiates activation of pro-**MMP**-2 and **integrin** α vβ3 promotes maturation of **MMP**-2 in human breast carcinoma cells in relation to motility)

IT Neuroglia
(glioma; **MT1-MMP** initiates activation of pro-**MMP**-2 and **integrin** α vβ3 promotes maturation of **MMP**-2 in human breast carcinoma cells in relation to motility)

IT **Integrins**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(α **v**.beta.3; **MT1-MMP** initiates activation of pro-**MMP**-2 and **integrin** α **v**.beta.3 promotes maturation of **MMP**-2 in human breast carcinoma cells in relation to motility)

IT 146480-35-5, **Matrix metalloproteinase**-2 148969-98-6, Pro-**MMP**-2 **161384-17-4**, **MT1-MMP**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**MT1-MMP** initiates activation of pro-**MMP**-2 and **integrin** α vβ3 promotes maturation of **MMP**-2 in human breast carcinoma cells in relation to motility)

IT 124861-55-8, TIMP-2
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**MT1-MMP** initiates activation of pro-**MMP**-2 and **integrin** α vβ3 promotes maturation of **MMP**-2 in human breast carcinoma cells in relation to motility)

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD

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IT **161384-17-4**, **MT1-MMP**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**MT1-MMP** initiates activation of pro-**MMP**-2 and **integrin** α vβ3 promotes maturation of **MMP**-2 in human breast carcinoma cells in relation to motility)
RN 161384-17-4 HCAPLUS
CN Proteinase, matrix metallo-, MT-MMP-1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L54 ANSWER 6 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2001:31742** HCAPLUS
DN **134:99591**
ED Entered STN: 12 Jan 2001
TI Diagnostics and therapeutics for arterial wall disruptive disorders
IN Hageman, Gregory S.
PA University of Iowa Research Foundation, USA
SO PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM G01N033-68
CC 15-8 (Immunochemistry)
Section cross-reference(s): 1, 3, 9, 14
FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001002866	A1	20010111	WO 2000-US4583	20000222 <--

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ,

BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1153301 A1 20011114 EP 2000-915841 20000222 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

JP 2003506016 T2 20030218 JP 2001-508612 20000222 <--
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PRAI US 1999-120668P P 19990219 <--
US 1999-120822P P 19990219 <--
US 1999-123052P P 19990305 <--
WO 2000-US4583 W 20000222 <--

AB The invention provides diagnostics, therapeutics and drug **screening** assays for arterial wall disruptive disorders, based on the discovery of a high level of correlation between the incidence of arterial wall disruptive disorders and the incidence of Age Related Macular Degeneration (AMD). In one embodiment, the arterial wall disruptive disorder is an aortic aneurysm.

ST arterial wall disruptive disorder marker model

IT Amyloid
Apolipoproteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Rat
(Anidjar/Dobrin; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Big H3; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C-reactive; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD100; diagnostics and therapeutics for arterial wall disruptive disorders)

IT CD1 (antigen)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD1a; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD83; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Genetic markers
(D2S2352 and D2S1364; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Nucleic acid amplification (method)
(DNA, anal.; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Apolipoproteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(E; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HLA-DR; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Heat-shock proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HSP 70; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ICAM-1 (intercellular adhesion mol. 1); diagnostics and therapeutics for arterial wall disruptive disorders)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LTLP; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MFAP-1; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MFAP-2; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MHC (major histocompatibility complex); diagnostics and therapeutics for arterial wall disruptive disorders)

IT Amyloid
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(P; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PECAM-1; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PI-1 protein; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PI-2 protein; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PLOD; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Proteins, specific or class

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RAIDD or death adaptor protein; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(S-100; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Aneurysm
(abdominal aortic aneurysm; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(acute-phase; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Diagnosis
(agents; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Animal tissue
(anal.; diagnostics and therapeutics for arterial wall disruptive disorders)

IT RNA
RL: AMX (Analytical matrix); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(anal.; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Radiography
(angiog., fundus fluorescein; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Interleukin 13
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antagonists; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Aneurysm
(aortic; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Artery, disease
(arterial wall disruptive disorder; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Antibodies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(autoantibodies; diagnostics and therapeutics for arterial wall disruptive disorders)

IT **Integrins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(b-1; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Drug delivery systems
(carriers; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cell death protein; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Eye
(choroid, fibrosis; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Fibrosis
(choroidal; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Cell activation
Cell differentiation
Cell migration
Cell proliferation
(dendritic cell; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Disease, animal
(dense deposit disease; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Test kits
(diagnostic; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Aging, animal
Alleles
Amyloidosis
Anti-inflammatory agents
Atherosclerosis
Blood analysis
Chromosome
Disease models
Drug screening
Genetic markers
Genetic polymorphism
Immunoassay
Infection
Leukocyte
Mammal (Mammalia)
Susceptibility (genetic)
Urine analysis
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Nucleic acids
RL: AMX (Analytical matrix); BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT DNA
RL: AMX (Analytical matrix); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Antibodies
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT CD antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT CD14 (antigen)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT CD4 (antigen)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT CD45 (antigen)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)

IT CD68 (antigen)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT CD80 (antigen)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT CD86 (antigen)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Chemokines
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Clusterin
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Collagens, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Complement receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Cytokines
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Elastins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Fibrillins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Fibrinogens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Gene, animal
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Heat-shock proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Immune complexes
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Immunoglobulins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Interleukin 1
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Interleukin 10
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Interleukin 12
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Interleukin 3
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Interleukin 4
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Interleukin 6
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Interleukins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT **LFA-1 (antigen)**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT LFA-3 (antigen)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Thrombospondins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Tumor necrosis factors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Vitronectin
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
IT Granulation tissue
(disciform; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Macaca irus
Monkey
(disease model; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Connective tissue
(disease, inherited; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Aneurysm
(dissecting; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Biomarkers (biological responses)
(drusen-associated; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Disease, animal
(elastosis; diagnostics and therapeutics for arterial wall disruptive

disorders)
IT Electrochemical analysis
(electrooculogram; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Electrochemical analysis
(electroretinogram; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emilin; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Glycoproteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fibulins; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ficolin; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Photography
(fundus; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Chromosome
(human 2; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Biochemical molecules
(immune-associated; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lamins; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Scanning microscopy
(laser scanning microscopy, canning laser ophthalmoscopy; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Immunoglobulins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(light chains, λ and κ; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Eye, disease
(macula, degeneration; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Fibrosis
(macula; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Vision
(measurement; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Neuroglia
(microglia, retinal; diagnostics and therapeutics for arterial wall disruptive disorders)
IT **Angiogenesis**
(neovascularization, retinal; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Aneurysm
(peripheral; diagnostics and therapeutics for arterial wall disruptive disorders)
IT Eye

(pigment epithelium, subretinal pigmented epithelial spacc; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Dendritic cell
(proliferation; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Eye
(retina, antigen; diagnostics and therapeutics for arterial wall disruptive disorders)

IT **Eye, disease**
(**retina, neovascularization**; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Cell death
(retinal pigment epithelium; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Repetitive DNA
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tandem, short; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Artery, disease
(thoracic aorta, aneurysm; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Animal
(transgenic; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Collagens, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type VI; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Aneurysm
(visceral; diagnostics and therapeutics for arterial wall disruptive disorders)

IT Microglobulins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β2-; diagnostics and therapeutics for arterial wall disruptive disorders)

IT 9004-06-2, Elastase
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HME or human macrophage elastase; diagnostics and therapeutics for arterial wall disruptive disorders)

IT 9054-89-1
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(copper-zinc-containing; diagnostics and therapeutics for arterial wall disruptive disorders)

IT 9001-26-7, Prothrombin 9001-29-0, Factor X 9001-92-7, **Protease** 9004-08-4, Cathepsin 9059-25-0, Lysyl oxidase 37205-61-1, **Protease** inhibitor 60267-61-0, Ubiquitin 62031-54-3, FGF 62683-29-8, CSF 80295-41-6, Complement C3 80295-53-0, Complement C5 80295-59-6, Complement C9 81627-83-0, M-CSF 82986-89-8, Complement C5b9 83869-56-1, GM-CSF 86102-31-0, TIMP 140879-24-9, Proteasome 141256-43-1, Antichymotrypsin 141907-41-7 **161384-17-4**, **MMP-14**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)

IT 92899-39-3 319937-31-0 319937-32-1 319937-33-2 319937-34-3 319937-35-4 319937-36-5 319937-37-6 319937-38-7 319937-39-8 319937-40-1 319937-41-2 319937-42-3 319937-43-4 319937-44-5 319937-45-6 319937-46-7 319937-47-8 319937-48-9 319937-49-0

319937-50-3 319937-51-4 319937-52-5 319937-53-6
RL: PRP (Properties)
(unclaimed sequence; diagnostics and therapeutics for arterial wall disruptive disorders)
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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IT **161384-17-4, MMP-14**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostics and therapeutics for arterial wall disruptive disorders)
RN 161384-17-4 HCAPLUS
CN Proteinase, matrix metallo-, MT-MMP-1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L54 ANSWER 7 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2001:14693** HCAPLUS
DN **134:324533**
ED Entered STN: 08 Jan 2001
TI Ligation of α 4β1 **integrin** on human intestinal mucosal mesenchymal cells selectively up-regulates **membrane type-1 matrix metalloproteinase** and confers a migratory phenotype
AU Pender, Sylvia L. F.; Salmela, Mikko T.; Monteleone, Giovanni; Schnapp, Denni; McKenzie, Catriona; Spencer, Jo; Fong, Sherman; Saarialho-Kere, Ulpu; MacDonald, Thomas T.
CS Centre for Infection, Allergy, Inflammation and Repair, University of Southampton School of Medicine, Southampton, SO 16 6YD, UK
SO American Journal of Pathology (**2000**), 157(6), 1955-1962
CODEN: AJPAA4; ISSN: 0002-9440
PB American Society for Investigative Pathology
DT Journal
LA English
CC 14-7 (Mammalian Pathological Biochemistry)
AB Human intestinal lamina propria mesenchymal cells show high surface expression of the α 4β1 **integrin.** Ligation of α 4β1 on mesenchymal cell lines with an activating **monoclonal** anti-α 4 antibody or vascular cell adhesion mol.-Ig (VCAM-IgG) leads to the appearance of activated forms of gelatinase A in culture supernatants, and the de novo expression of activated **membrane type-1-matrix metalloproteinase** (**MT1-MMP**). In functional assays, signaling through α 4β1 results in an increased capacity of mesenchymal cells to migrate through an artificial extracellular **matrix**, an effect inhibitable by excess tissue inhibitor of **metalloproteinase**-2. In organ cultures of human intestine, VCAM-IgG also up-regulates **MT1-MMP**, and in mucosal ulcers of inflammatory bowel disease patients, **MT1-MMP** transcripts are abundant, coincident with expression of VCAM-1 on cells at the ulcer margin. Collectively these results suggest that . **alpha.**4β1-induced up-regulation of **MT1-MMP** may be a crucial factor in the migration of mesenchymal cells into ulcer beds during restitution of diseased gut mucosa.
ST ligation alpha4beta1 **integrin** intestinal mucosal mesenchyme MT1MMP **metalloproteinase** migration; **membrane type 1 matrix metalloproteinase** intestine mesenchyme alpha4beta1 **integrin**

IT Gene, animal
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**MT-MMP**-1; ligation of α 4β1 **integrin** on human intestinal mucosal mesenchymal cells up-regulates **membrane type-1 matrix metalloproteinase** and confers a migratory phenotype in relation to migration into ulcer beds during restitution)

IT mRNA
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PROC (Process)
(**MT-MMP**-1; ligation of α 4β1 **integrin** on human intestinal mucosal mesenchymal cells up-regulates **membrane type-1 matrix metalloproteinase** and confers a migratory phenotype in relation to migration into ulcer beds during restitution)

IT Cell adhesion molecules
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(VCAM-1; ligation of α 4β1 **integrin** on human intestinal mucosal mesenchymal cells selectively up-regulates **membrane type-1 matrix metalloproteinase** and confers a migratory phenotype in relation to migration into ulcer beds during restitution and)

IT Transcriptional regulation
(activation; ligation of α 4β1 **integrin** on human intestinal mucosal mesenchymal cells selectively up-regulates **membrane type-1 matrix metalloproteinase** and confers a migratory phenotype in relation to migration into ulcer beds during restitution)

IT Intestine, disease
(inflammatory; ligation of α 4β1 **integrin** on human intestinal mucosal mesenchymal cells selectively up-regulates **membrane type-1 matrix metalloproteinase** and confers a migratory phenotype in relation to migration into ulcer beds during restitution and)

IT Animal cell line
Cell migration
Phenotypes
(ligation of α 4β1 **integrin** on human intestinal mucosal mesenchymal cells selectively up-regulates **membrane type-1 matrix metalloproteinase** and confers a migratory phenotype in relation to migration into ulcer beds during restitution)

IT Signal transduction, biological
Wound healing
(ligation of α 4β1 **integrin** on human intestinal mucosal mesenchymal cells selectively up-regulates **membrane type-1 matrix metalloproteinase** and confers a migratory phenotype in relation to migration into ulcer beds during restitution and)

IT Extracellular **matrix**
(migration through; ligation of α 4β1 **integrin** on human intestinal mucosal mesenchymal cells up-regulates **membrane type-1 matrix metalloproteinase** and confers a migratory phenotype in relation to migration into ulcer beds during restitution)

IT Intestine
(mucosa; ligation of α 4β1 **integrin** on human intestinal mucosal mesenchymal cells selectively up-regulates **membrane type-1 matrix**

metalloproteinase and confers a migratory phenotype in relation to migration into ulcer beds during restitution)

IT Intestine, disease
(ulcer; ligation of α 4β1 **integrin** on human intestinal mucosal mesenchymal cells selectively up-regulates **membrane type-1 matrix** **metalloproteinase** and confers a migratory phenotype in relation to migration into ulcer beds during restitution)

IT **Integrins**
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(α 4β1; ligation of α 4β1 **integrin** on human intestinal mucosal mesenchymal cells selectively up-regulates **membrane type-1 matrix metalloproteinase** and confers a migratory phenotype in relation to migration into ulcer beds during restitution)

IT **161384-17-4, Matrix metalloproteinase MT-MMP-1**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(ligation of α 4β1 **integrin** on human intestinal mucosal mesenchymal cells selectively up-regulates **membrane type-1 matrix** **metalloproteinase** and confers a migratory phenotype in relation to migration into ulcer beds during restitution)

IT 146480-35-5, Gelatinase A
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(ligation of α 4β1 **integrin** on human intestinal mucosal mesenchymal cells selectively up-regulates **membrane type-1 matrix** **metalloproteinase** and confers a migratory phenotype in relation to migration into ulcer beds during restitution and)

IT 79955-99-0, Stromelysin 1 124861-55-8, **Proteinase** inhibitor, TIMP-2 140208-24-8, **Proteinase** inhibitor, TIMP-1 146480-36-6, Gelatinase B
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(ligation of α 4β1 **integrin** on human intestinal mucosal mesenchymal cells selectively up-regulates **membrane type-1 matrix** **metalloproteinase** and confers a migratory phenotype in relation to migration into ulcer beds during restitution and)

IT 9001-12-1, Collagenase
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(type 1; ligation of α 4β1 **integrin** on human intestinal mucosal mesenchymal cells up-regulates **membrane type-1 matrix** **metalloproteinase** and confers a migratory phenotype in relation to migration into ulcer beds during restitution)

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IT **161384-17-4**, **Matrix metalloproteinase MT-MMP-1**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(ligation of α 4β1 **integrin** on human intestinal mucosal mesenchymal cells selectively up-regulates **membrane type-1 matrix metalloproteinase** and confers a migratory phenotype in relation to migration into ulcer beds during restitution)

RN 161384-17-4 HCAPLUS
CN Proteinase, matrix metallo-, MT-MMP-1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L54 ANSWER 8 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2001:3193** HCAPLUS
DN **134:129112**
ED Entered STN: 02 Jan 2001
TI Adhesion-dependent control of **matrix metalloproteinase** -2 activation in human capillary endothelial cells
AU Yan, Li; Moses, Marsha A.; Huang, Sui; Ingber, Donald E.

CS Departments of Surgery and Children's Hospital, Harvard Medical School, Boston, MA, 02115, USA
SO Journal of Cell Science (**2000**), 113(22), 3979-3987
CODEN: JNCSAI; ISSN: 0021-9533
PB Company of Biologists Ltd.
DT Journal
LA English
CC 13-6 (Mammalian Biochemistry)
AB The growth and regression of capillary blood vessels during **angiogenesis** is greatly influenced by changes in the activity of **matrix metalloproteinases** (**MMPs**), which selectively degrade extracellular **matrix** (ECM) and thereby modulate capillary endothelial cell shape, growth and viability. However, changes in cell-ECM binding and cell spreading have also been reported to alter **MMP** secretion and activation. Studies were carried out to determine whether changes in **integrin** binding or cell shape feed back to alter **MMP**-2 processing in human capillary endothelial (HCE) cells. Catalytic processing of proMMP-2 to active **MMP**-2 progressively decreased when HCE cells were cultured on dishes coated with increasing densities of fibronectin (FN), which promote both **integrin** binding and cell spreading. Conversely, the highest levels of active **MMP**-2 were detected in round cells cultured on low FN. When measured 24 h after plating, this increase in active **MMP**-2 was accompanied by a concomitant rise in mRNA and protein levels for the membrane-type 1 **MMP** (**MT1-MMP**), which catalyzes the **cleavage** of proMMP-2. To determine whether proMMP-2 processing was controlled directly by **integrin** binding or indirectly by associated changes in cell shape, round cells on low FN were allowed to bind to microbeads (4.5 μm diameter) coated with a synthetic RGD peptide or FN; these induce local **integrin** receptor clustering without altering cell shape. ProMMP-2 activation was significantly decreased within minutes after bead binding in these round cells, prior to any detectable changes in expression of **MT1-MMP**, whereas binding of beads coated with control ligands for other transmembrane receptors had no effect. This inhibitory effect was mimicked by microbeads coated with activating antibodies against . **alpha.**Vβ3 and β1 **integrins**, suggesting a direct role for these cell-surface ECM receptors in modulating proMMP-2 activation. Similar inhibition of proMMP-2 processing by **integrin** binding, independent of cell spreading, was demonstrated in cells that were cultured on small, microfabricated adhesive islands that prevented cell spreading while presenting a high FN d. directly beneath the cell. Interestingly, when spread cells were induced to round up from within by disrupting their actin cytoskeleton using cytochalasin D, proMMP-2 processing did not change at early times; however, increases in **MT1-MMP** mRNA levels and **MMP**-2 activation could be detected by 18 h. Taken together, these results suggest the existence of two phases of **MMP**-2 regulation in HCE cells when they adhere to ECM: (1) a quick response, in which **integrin** clustering alone is sufficient to rapidly inhibit processing of proMMP-2 and (2) a slower response, in which subsequent cell spreading and changes in the actin cytoskeleton feed back to decrease expression of **MT1-MMP** mRNA and, thereby, further suppress cellular proteolytic activity.
ST MMP2 capillary endothelium extracellular **matrix** adhesion; **integrin** actin cytoskeleton **matrix** **metalloproteinase** MTMMP1 cell shape **angiogenesis**
IT Spreading
(biol.; **integrins** and actin cytoskeleton in adhesion-dependent control of **matrix** **metalloproteinase**-2 activation by downregulating membrane-type 1 **metalloproteinase** in human capillary endothelial cells)
IT Capillary vessel
(endothelium; **integrins** and actin cytoskeleton in

adhesion-dependent control of **matrix metalloproteinase**-2 activation by downregulating membrane-type 1 **metalloproteinase** in human capillary endothelial cells)

IT Cell adhesion
Cell morphology
Cytoskeleton
Extracellular **matrix**
(**integrins** and actin cytoskeleton in adhesion-dependent control of **matrix metalloproteinase**-2 activation by downregulating membrane-type 1 **metalloproteinase** in human capillary endothelial cells)

IT **Angiogenesis**
(**integrins** and actin cytoskeleton in adhesion-dependent control of **matrix metalloproteinase**-2 activation by downregulating membrane-type 1 **metalloproteinase** in human capillary endothelial cells in relation to)

IT **Integrins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(α **v**.beta.3; **integrins** and actin cytoskeleton in adhesion-dependent control of **matrix metalloproteinase**-2 activation by downregulating membrane-type 1 **metalloproteinase** in human capillary endothelial cells)

IT **Integrins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(β1; **integrins** and actin cytoskeleton in adhesion-dependent control of **matrix metalloproteinase**-2 activation by downregulating membrane-type 1 **metalloproteinase** in human capillary endothelial cells)

IT **161384-17-4**, **Membrane-type 1 matrix metalloproteinase**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**integrins** and actin cytoskeleton in adhesion-dependent control of **matrix metalloproteinase**-2 activation by downregulating membrane-type 1 **metalloproteinase** in human capillary endothelial cells)

IT 148969-98-6, Promatrix **metalloproteinase**-2
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**integrins** and actin cytoskeleton in adhesion-dependent control of **matrix metalloproteinase**-2 activation by downregulating membrane-type 1 **metalloproteinase** in human capillary endothelial cells)

IT 146480-35-5, **Matrix metalloproteinase**-2
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(**integrins** and actin cytoskeleton in adhesion-dependent control of **matrix metalloproteinase**-2 activation by downregulating membrane-type 1 **metalloproteinase** in human capillary endothelial cells)

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IT **161384-17-4**, **Membrane-type 1 matrix metalloproteinase**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**integrins** and actin cytoskeleton in adhesion-dependent control of **matrix metalloproteinase**-2 activation by downregulating membrane-type 1 **metalloproteinase** in human capillary endothelial cells)

RN 161384-17-4 HCAPLUS
CN Proteinase, matrix metallo-, MT-MMP-1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L54 ANSWER 9 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2000:435713** HCAPLUS
DN **133:308362**
ED Entered STN: 29 Jun 2000
TI Expression of **integrin** α vβ3 correlates with activation of **membrane-type matrix metalloproteinase-1** (**MT1-MMP**) and **matrix metalloproteinase**-2 (**MMP**-2) in human melanoma cells in vitro and in vivo
AU Hofmann, Uta B.; Westphal, Johan R.; Van Kraats, Annemieke A.; Ruiter, Dirk J.; Van Muijen, Goos N. P.
CS Department of Pathology, University Hospital, Nijmegen, 6500 HB, Neth.
SO International Journal of Cancer (**2000**), 87(1), 12-19
CODEN: IJCNAW; ISSN: 0020-7136
PB Wiley-Liss, Inc.
DT Journal
LA English
CC 14-1 (Mammalian Pathological Biochemistry)
AB Activation of **matrix metalloproteinase**-2 (**MMP**-2) is mediated by binding to the complex of **membrane-type matrix metalloproteinase-1** (**MT1-MMP**) with tissue inhibitor of **MMP**-2 (TIMP-2) on the cell surface. Binding of **MMP**-2 to **integrin** α vβ3 has been implicated in presenting activated **MMP**-2 on the cell surface of invasive cells, but interactions with the **MT1-MMP**-TIMP-2 system have not been considered. Therefore, we studied the expression and interaction of **MT1-MMP**, **MMP**-2 and TIMP-2 in the α vβ3-neg. melanoma cell line BLM and in its β3-transfected, α vβ3-expressing counterpart BLM-β3, both on cell lines and in xenografts. Total expression levels of **MMP**-2, **MT1-MMP** and TIMP-2 did not differ markedly between the α vβ3-neg. and . **alpha.**vβ3-pos. cells. Remarkable differences, however, exist in the presence of active **MMP**-2 and **MT1-MMP.** Zymog. on cell lysates revealed that active **MMP**-2 was restricted to α vβ3-pos. cell line and clearly accumulated in xenografts derived from the BLM-β3 cells, confirming the relevance of this **integrin** for **MMP**-2 function. Western blotting of cell lysates showed that processing of proMT1-**MMP** to the activated form was enhanced in BLM-β3. The ratio of active and inactive **MT1-MMP** was 3-fold higher in the β3-transfectants. Immunofluorescence double-labeling followed by confocal laser microscopy showed co-localization of **MT1-MMP** and α vβ3 on BLM-β3 cells. In xenografts from BLM-β3 cells, active **MT1-MMP** was markedly increased. Our results demonstrate that expression of . **alpha.**vβ3 in cell lines and xenografts was accompanied by an accumulation of active **MT1-MMP** and **MMP**-2. Furthermore, **MT1-MMP** and α vβ3 are co-localized on the cell membrane of tumor cells. These findings suggest that activated **MT1-MMP** co-localized with . **alpha.**vβ3 may be involved in activation of **.alpha** .vβ3-bound **MMP**-2.
ST **integrin matrix metalloproteinase** melanoma cell membrane
IT Cell membrane
Melanoma
(**integrin** α vβ3 expression correlates with activation of **membrane-type matrix metalloproteinase-1** and **matrix metalloproteinase**-2 in human melanoma cells)

IT **Integrins**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(α **v**.beta.3; **integrin** α **v**.beta.3 expression correlates with activation of **membrane-type matrix metalloproteinase-1** and **matrix metalloproteinase**-2 in human melanoma cells)
IT 124861-55-8, TIMP-2 146480-35-5, **Matrix metalloproteinase**-2 **161384-17-4**, **Membrane-type matrix metalloproteinase-1**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**integrin** α vβ3 expression correlates with activation of **membrane-type matrix metalloproteinase-1** and **matrix metalloproteinase**-2 in human melanoma cells)
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IT **161384-17-4**, **Membrane-type matrix metalloproteinase-1**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**integrin** α vβ3 expression correlates with activation of **membrane-type matrix metalloproteinase-1** and **matrix metalloproteinase**-2 in human melanoma cells)
RN 161384-17-4 HCAPLUS
CN Proteinase, matrix metallo-, MT-MMP-1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L54 ANSWER 10 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2000:203347** HCAPLUS
DN **133:118149**
ED Entered STN: 30 Mar 2000
TI Functional activation of **integrin** α vβ3 in tumor cells expressing **membrane-type 1 matrix metalloproteinase**
AU Deryugina, Elena I.; Bourdon, Mario A.; Jungwirth, Karli; Smith, Jeffrey W.; Strongin, Alex Y.

CS La Jolla Institute for Experimental Medicine, La Jolla, CA, 92037, USA
SO International Journal of Cancer (**2000**), 86(1), 15-23
CODEN: IJCNAW; ISSN: 0020-7136
PB Wiley-Liss, Inc.
DT Journal
LA English
CC 14-1 (Mammalian Pathological Biochemistry)
AB **Matrix metalloproteinases** (**MMPs**) and **integrins** have been implicated in a variety of processes involved in tumor progression. To evaluate the individual roles of **integrin** α vβ3 and **membrane-type 1 matrix metalloproteinase** (**MT1-MMP**), as well as the effects of their joint expression on tumor cell functions, MCF7 breast carcinoma cells were transfected stably with either the **MT1-MMP**, the β3 **integrin subunit** or both **MT1-MMP** and β3 cDNAs. **MT1-MMP** expression is accompanied by the functional activation of **integrin** . **alpha.**vβ3, thereby increasing vitronectin-mediated adhesion and migration of MCF7 cells transfected with **MT1-MMP** and **integrin** α vβ3. **MT1-MMP**-dependent functional activation of α vβ3 correlates with modification(s) of the β3 **subunit**, including its higher **electrophoretic** mobility and affected the LM609-binding site. MCF7 cells jointly expressing **MT1-MMP** and α vβ3 were the most efficient in adhesion to the **recombinant** C-terminal domain of **MMP**-2 as well as in generating soluble and cell surface associated mature **MMP**-2 enzyme. These findings suggest a mechanism of selective docking of **MMP**-2 at tumor cell surfaces, specifically at the sites that include **MT1-MMP** and activated **integrin** . **alpha.**vβ3. These mechanisms may provide a link between spatial regulation of focal proteolysis by the cell surface associated **MMPs** and the regulation of **integrin**-mediated motility of tumor cells.
ST **integrin** alphavbeta3 **matrix metalloproteinase** 1 cancer
IT Animal cell line
(MCF-7; functional activation of **integrin** α vβ3 in tumor cells expressing **membrane-type 1 matrix metalloproteinase**)
IT Mammary gland
(carcinoma; functional activation of **integrin** α vβ3 in tumor cells expressing **membrane-type 1 matrix metalloproteinase**)
IT Vitronectin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(functional activation of **integrin** α vβ3 in tumor cells expressing **membrane-type 1 matrix metalloproteinase**)
IT **Integrins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(α **v**.beta.3; functional activation of **integrin** α **v**.beta.3 in tumor cells expressing **membrane-type 1 matrix metalloproteinase**)
IT **161384-17-4, Membrane-type 1 matrix metalloproteinase**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(functional activation of **integrin** α vβ3
in tumor cells expressing **membrane-type 1**
matrix metalloproteinase)
IT 146480-35-5, **Matrix metalloproteinase** 2
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(functional activation of **integrin** α vβ3
in tumor cells expressing **membrane-type 1**
matrix metalloproteinase)
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
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IT **161384-17-4**, **Membrane-type 1**
matrix metalloproteinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(functional activation of **integrin** α vβ3
in tumor cells expressing **membrane-type 1**
matrix metalloproteinase)
RN 161384-17-4 HCAPLUS
CN Proteinase, matrix metallo-, MT-MMP-1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L54 ANSWER 11 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2000:9675** HCAPLUS
DN **132:135328**
ED Entered STN: 06 Jan 2000
TI Role of **membrane-type matrix**
metalloproteinase 1 (**MT-1-**
MMP), **MMP**-2, and its inhibitor in nephrogenesis
AU Kanwar, Yashpal S.; Ota, Kosuke; Yang, Qiwei; Wada, Jun; Kashihara, Naoki; Tian, Yufeng; Wallner, Elisabeth I.
CS Department of Pathology, Northwestern University Medical School, Chicago, IL, 60611, USA
SO American Journal of Physiology (**1999**), 277(6, Pt. 2), F934-F947
CODEN: AJPHAP; ISSN: 0002-9513
PB American Physiological Society
DT Journal
LA English
CC 13-3 (Mammalian Biochemistry)
AB Extracellular **matrix** (ECM) proteins, their **integrin**

receptors, and **matrix metalloproteinases (MMPs**
), the ECM-degrading enzymes, are believed to be involved in various biol.
processes, including embryogenesis. In the present study, we investigated
the role of membrane type **MMP**, **MT-1-**
MMP, an activator pro-**MMP**-2, in metanephric development.
Also, its relationship with **MMP**-2 and its inhibitor, TIMP-2, was
studied. Since mRNAs of **MT-1-MMP** and
MMP-2 are resp. expressed in the ureteric bud epithelia and
mesenchyme, they are ideally suited for juxtacrine/paracrine interactions
during renal development. Northern blot analyses revealed a single
.apprx.4.5-kb mRNA transcript of **MT-1-MMP**,
and its expression was developmentally regulated. Inclusion of **MT**
-1-MMP antisense oligodeoxynucleotide (ODN) in the
culture media induced dysmorphogenetic changes in the embryonic
metanephros. **MMP**-2 antisense ODN also induced similar changes,
but they were relatively less; on the other hand TIMP-2 antisense ODN
induced a mild increase in the size of explants. Concomitant exposure of
MT-1-MMP and **MMP**-2 antisense ODNs
induced profound alterations in the metanephros. Treatment of TIMP-2
antisense ODN to metanephros exposed to **MT-1-**
MMP/**MMP**-2 antisense notably restored the morphol. of the
explants. Specificity of the **MT-1-MMP**
antisense ODN was reflected in the selective decrease in its mRNA and
protein expression. The **MT-1-MMP** antisense
ODN also resulted in a failure in the activation of pro-**MMP**-2 to
MMP-2. These findings suggest that the trimacromol. complex of
MT-1-MMP:**MMP**-2:TIMP-2 modulates the
organogenesis of the metanephros, conceivably by mediating
paracrine/juxtacrine epithelial:mesenchymal interactions.

ST **matrix metalloproteinase** TIMP metanephros kidney
embryogenesis; **MMP** MTMMP1 nephrogenesis kidney epithelium
mesenchyme

IT Embryo, animal
(embryogenesis; **membrane-type matrix**
metalloproteinase 1 and **MMP**-2 and its
inhibitor in nephrogenesis)

IT Kidney
(epithelium, ureteric bud; **membrane-type**
matrix metalloproteinase 1 and **MMP**
-2 and its inhibitor in nephrogenesis)

IT Embryo, animal
(fetus; **membrane-type matrix**
metalloproteinase 1 and **MMP**-2 and its
inhibitor in nephrogenesis)

IT Extracellular **matrix**
Morphogenesis, animal
Newborn
(**membrane-type matrix**
metalloproteinase 1 and **MMP**-2 and its
inhibitor in nephrogenesis)

IT Kidney
(mesenchyme, ureteric bud; **membrane-type**
matrix metalloproteinase 1 and **MMP**
-2 and its inhibitor in nephrogenesis in relation to)

IT Kidney
(metanephros; **membrane-type matrix**
metalloproteinase 1 and **MMP**-2 and its
inhibitor in nephrogenesis)

IT 124861-55-8, TIMP-2 146480-35-5, **Matrix**
metalloproteinase 2 **161384-17-4**, **Membrane-**
type matrix metalloproteinase 1
RL: BAC (Biological activity or effector, except adverse); BOC (Biological
occurrence); BPR (Biological process); BSU (Biological study,

unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**membrane-type matrix metalloproteinase 1** and **MMP**-2 and its inhibitor in nephrogenesis)
IT 148969-98-6, Pro-**MMP**-2
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**membrane-type matrix metalloproteinase 1** and **MMP**-2 and its inhibitor in nephrogenesis)
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IT **161384-17-4**, **Membrane-type matrix metalloproteinase 1**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**membrane-type matrix metalloproteinase 1** and **MMP**-2 and its inhibitor in nephrogenesis)
RN 161384-17-4 HCAPLUS
CN Proteinase, matrix metallo-, MT-MMP-1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L54 ANSWER 12 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1999:672439** HCAPLUS
DN **132:2764**
ED Entered STN: 22 Oct 1999
TI Fibronectin upregulates gelatinase B (**MMP**-9) and induces coordinated expression of gelatinase A (**MMP**-2) and its activator **MT1-MMP** (**MMP-14**) by human T lymphocyte cell lines. A process repressed through RAS/MAP kinase signaling pathways
AU Esparza, Jordi; Vilardell, Carme; Calvo, Javier; Juan, Manel; Vives, Jordi; Urbano-Marquez, Alvaro; Yague, Jordi; Cid, Maria C.

CS Departments of Internal Medicine and Immunology, Hospital Clinic, IDIBAPS (Institut d'Investigacions Biomediques August Pi i Sunyer), University of Barcelona, Barcelona, Spain
SO Blood (**1999**), 94(8), 2754-2766
CODEN: BLOOAW; ISSN: 0006-4971
PB W. B. Saunders Co.
DT Journal
LA English
CC 15-10 (Immunochemistry)
AB T-lymphocyte migration into tissues requires focal degradation of the basement membrane. Here, the authors show that transient adherence to fibronectin induces the production of activated forms of **matrix metalloproteinase**-2 (**MMP**-2) and **MMP**-9, as well as downregulation of tissue inhibitor of **metalloproteinase**-2 (TIMP-2) by T-cell lines. **MMP**-2 activation was likely achieved by inducing a coordinated expression of **membrane-type matrix metalloproteinase-1** (**MMP-14**), a major activator of **MMP**-2. Blocking **monoclonal** antibodies against α 4, **.alpha** .5, and α v **integrins** strongly reduced **MMP**-2 and **MMP**-9 production induced by fibronectin. Disrupting actin cytoskeleton organization by cytochalasin D strongly enhanced fibronectin-induced **MMP**-2 and **MMP**-9 expression. Inhibiting Src tyrosine kinases with herbimycin A reduced **MMP**-2 and **MMP**-9 production with no effect on cell attachment. By contrast, G-protein inhibition by pertussis toxin, or transfection with a dominant neg. mutant of Ha-Ras strongly increased fibronectin-induced **MMP**-2 and **MMP**-9. Inhibition of PI3 kinase, MAP kinase (MEK1), or p38 MAP kinase by wortmannin, PD 98059, or SB 202190, resp., strongly promoted fibronectin-induced MMP2 and **MMP**-9. Cells at high d. lost their ability to synthesize **MMP**-2 and **MMP**-9 in response to fibronectin and **MMP** expression was restored by transfection with a dominant-neg. mutant of Ha-Ras or by treatment with wortmannin, PD 98059, or SB 202190. Apparently, adhesion to fibronectin transduces both stimulatory (through Src-type tyrosine kinases) and inhibitory signals (through Ras/MAPKinase signaling pathways) for **MMP**-2 and **MMP**-9 expression by T cells and their relative predominance is regulated by addnl. stimuli related to cell adhesion, motility, and growth.
ST fibronectin gelatinase T cell RAS MAP kinase signaling inflammation
IT Cell adhesion
Cell migration
Inflammation
Signal transduction, biological
T cell (lymphocyte)
(fibronectin upregulates gelatinase B (**MMP**-9) and induces coordinated expression of gelatinase A (**MMP**-2) and activator **MT1-MMP** (**MMP-14**) by human T cells, a process repressed via RAS/MAP kinase signaling)
IT Fibronectins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(fibronectin upregulates gelatinase B (**MMP**-9) and induces coordinated expression of gelatinase A (**MMP**-2) and activator **MT1-MMP** (**MMP-14**) by human T cells, a process repressed via RAS/MAP kinase signaling)
IT Ras proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(p21c-Ha-ras; fibronectin upregulates gelatinase B (**MMP**-9) and induces coordinated expression of gelatinase A (**MMP**-2) and activator **MT1-MMP** (**MMP-14**) by human T cells, a process repressed via RAS/MAP kinase signaling)

IT G proteins (guanine nucleotide-binding proteins)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pertussis toxin-sensitive; fibronectin upregulates gelatinase B (**MMP**-9) and induces coordinated expression of gelatinase A (**MMP**-2) and activator **MT1-MMP** (**MMP**-**14**) by human T cells, a process repressed via RAS/MAP kinase signaling)

IT **Integrins**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(α **v**; fibronectin upregulates gelatinase B (**MMP**-9) and induces coordinated expression of gelatinase A (**MMP**-2) and activator **MT1-MMP** (**MMP**-**14**) by human T cells, a process repressed via RAS/MAP kinase signaling)

IT **Integrins**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(α 4; fibronectin upregulates gelatinase B (**MMP**-9) and induces coordinated expression of gelatinase A (**MMP**-2) and activator **MT1-MMP** (**MMP-14**) by human T cells, a process repressed via RAS/MAP kinase signaling)

IT **Integrins**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(α **5**; fibronectin upregulates gelatinase B (**MMP**-9) and induces coordinated expression of gelatinase A (**MMP**-2) and activator **MT1-MMP** (**MMP**-**14**) by human T cells, a process repressed via RAS/MAP kinase signaling)

IT 115926-52-8, Phosphatidylinositol-3 kinase 141349-89-5 142805-58-1, MEK-1 kinase 165245-96-5, p38 Kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(fibronectin upregulates gelatinase B (**MMP**-9) and induces coordinated expression of gelatinase A (**MMP**-2) and activator **MT1-MMP** (**MMP-14**) by human T cells, a process repressed via RAS/MAP kinase signaling)

IT 124861-55-8, TIMP-2 146480-35-5, **MMP** 2 146480-36-6, **MMP** 9 **161384-17-4**, **MT1-MMP**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(fibronectin upregulates gelatinase B (**MMP**-9) and induces coordinated expression of gelatinase A (**MMP**-2) and activator **MT1-MMP** (**MMP-14**) by human T cells, a process repressed via RAS/MAP kinase signaling)

RE.CNT 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD

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IT **161384-17-4**, **MT1-MMP**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(fibronectin upregulates gelatinase B (**MMP**-9) and induces coordinated expression of gelatinase A (**MMP**-2) and activator **MT1-MMP** (**MMP-14**) by human T cells, a process repressed via RAS/MAP kinase signaling)

RN 161384-17-4 HCAPLUS
CN Proteinase, matrix metallo-, MT-MMP-1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L54 ANSWER 13 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1999:522013** HCAPLUS
DN **132:34121**

ED Entered STN: 20 Aug 1999
TI MMP2 activation by collagen I and concanavalin A in cultured human hepatic stellate cells
AU Theret, Nathalie; Lehti, Kaisa; Musso, Orlando; Clement, Bruno
CS Detoxication and Tissue Repair Unit, Universite de Rennes I, Rennes, 35043, Fr.
SO Hepatology (Philadelphia) (**1999**), 30(2), 462-468
CODEN: HPTLD9; ISSN: 0270-9139
PB W. B. Saunders Co.
DT Journal
LA English
CC 14-7 (Mammalian Pathological Biochemistry)
AB Fibrosis occurs in most chronic liver injuries and results from changes in the balance between synthesis and degradation of extracellular **matrix** components. In fibrotic livers, there is a markedly increased activity of **matrix metalloproteinase** 2 (MMP2), a major enzyme involved in extracellular **matrix** remodeling. We have previously shown that hepatic stellate cells secrete latent MMP2 and that MMP2 activation occurs in coculture of hepatic stellate cells and hepatocytes concomitantly with **matrix** deposition. In the present work we investigated the effects of various extracellular **matrix** components and Con A, an inducer of immune-mediated liver injuries, on MMP2 activation in cultured human hepatic stellate cells. Collagen I induced a dose-dependent MMP2 activation, which was not blocked by both actinomycin and cycloheximide. Collagen VI, laminin, and a reconstituted basement membrane (matrigel) were ineffective in inducing activation. Specific antibodies against the **subunits** of **.alpha** .2β1 **integrins**, the major collagen I receptor, induced partial inhibition of MMP2 activation. Treatment of cells with Con A resulted in a marked activation of MMP2 that correlated with the proteolytic processing of **MT1-MMP**, the MMP2 activator, from a Mr=60 kDa toward a Mr=43 kDa polypeptide. Actinomycin and cycloheximide inhibited the MMP2 activation induced by Con A. **Recombinant** tissue inhibitor of **metalloproteinase**-2 and the **MMP** inhibitor BB-3103, but not PMSF, blocked MMP2 activation induced by collagen I or Con A, and **MT1-MMP** processing to its Mr-43 kDa form. These results suggest that the accumulation of collagen I may specifically contribute to the remodeling of extracellular **matrix** in fibrotic livers by inducing MMP2 activation.
ST **metalloproteinase** 2 collagen I Con A liver fibrosis
IT Basement membrane
Extracellular **matrix**
Post-translational processing
(MMP2 activation by collagen I and Con A in cultured human hepatic stellate cells)
IT Laminins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(MMP2 activation by collagen I and Con A in cultured human hepatic stellate cells)
IT Liver, disease
(fibrosis; MMP2 activation by collagen I and Con A in cultured human hepatic stellate cells)
IT Liver, disease
(injury; MMP2 activation by collagen I and Con A in cultured human hepatic stellate cells)
IT Liver
(stellate cell; MMP2 activation by collagen I and Con A in cultured human hepatic stellate cells)
IT Collagens, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(type I; MMP2 activation by collagen I and Con A in cultured human

hepatic stellate cells)
IT Collagens, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(type VI; MMP2 activation by collagen I and Con A in cultured human hepatic stellate cells)
IT **Integrins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(α 2β1, **subunits**; MMP2 activation by collagen I and Con A in cultured human hepatic stellate cells)
IT 146480-35-5, Gelatinase A
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(MMP2 activation by collagen I and Con A in cultured human hepatic stellate cells)
IT 11028-71-0, Concanavalin A
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(MMP2 activation by collagen I and Con A in cultured human hepatic stellate cells)
IT **161384-17-4, Proteinase, matrix metallo-, MT-MMP-1**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(MMP2 activation by collagen I and Con A in cultured human hepatic stellate cells)
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IT **161384-17-4, Proteinase, matrix metallo-, MT-MMP-1**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(MMP2 activation by collagen I and Con A in cultured human hepatic stellate cells)
RN 161384-17-4 HCAPLUS
CN Proteinase, matrix metallo-, MT-MMP-1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L54 ANSWER 14 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1999:241796** HCAPLUS
DN **131:42896**
ED Entered STN: 20 Apr 1999
TI Ovarian carcinoma regulation of **matrix metalloproteinase** -2 and **membrane type 1 matrix metalloproteinase** through β1 **integrin**
AU Ellerbroek, Shawn M.; Fishman, David A.; Kearns, Alicia S.; Bafetti, Lisa M.; Stack, M. Sharon
CS Departments of Obstetrics and Gynecology and Cell and Molecular Biology, Northwestern University Medical School, Chicago, IL, 60611, USA
SO Cancer Research (**1999**), 59(7), 1635-1641
CODEN: CNREA8; ISSN: 0008-5472
PB AACR Subscription Office
DT Journal
LA English
CC 14-1 (Mammalian Pathological Biochemistry)
AB Culturing DOV 13 ovarian carcinoma cells on three-dimensional collagen lattice but not on thin-layer collagen induces processing of promatrix **metalloproteinase** (**MMP**)-2 to a Mr 62,000 form, suggesting that multivalent **integrin** aggregation may participate in **proteinase** regulation. To address the role of collagen-binding **integrins** in this event, the authors treated DOV 13 cells with soluble β1 **integrin** antibodies (**clones** P4C10 or 21C8) or β1 **integrin** antibodies immobilized on latex beads to promote **integrin** aggregation. Divalent ligation of β1 **integrins** with soluble P4C10 antibodies stimulated expression of pro-**MMP**-2 and its inhibitor, tissue inhibitor of **metalloproteinase**-2, whereas soluble 21C8 antibodies had no effect. Aggregation of β1 **integrins** with immobilized 21C8 or P4C10 antibodies stimulated **MMP**-dependent pro-**MMP**-2 activation and accumulation of a Mr 43,000 form of membrane type 1 **MMP** (**MT1-MMP**), a cell surface activator of pro-**MMP**-2, in cell exts. β1 **Integrin**-mediated **MMP**-2 activation required protein synthesis and tyrosine kinase signaling and was reduced by an inhibitor of gene transcription. Treatment of control cells with Con A stimulated **MMP**-dependent pro-**MMP**-2 activation and accumulation of Mr 55,000 and 43,000 forms of **MT1-MMP** in cell exts. Addition of either the **MMP** inhibitor GM-6001-X or exogenous tissue inhibitor of **metalloproteinase**-2 to Con A-treated cells resulted in loss of the Mr 43,000 form of **MT1-MMP** and accumulation of the Mr 55,000 form of the enzyme in cell exts., suggesting that the Mr 43,000 form is a product of **MMP**-dependent Mr 55,000 **MT1-MMP** proteolysis. Together, these data suggest that β1 **integrin** stimulation of pro-**MMP**-2 activation involves **MT1-MMP** posttranslational processing and requires multivalent **integrin** aggregation.
ST **matrix metalloproteinase** beta1 **integrin** ovarian carcinoma
IT Ovary, neoplasm
(carcinoma; ovarian carcinoma regulation of **matrix metalloproteinase**-2 and **membrane type 1 matrix metalloproteinase** through β1

integrin)
IT Neoplasm
(metastasis, ovarian carcinoma; ovarian carcinoma regulation of **matrix metalloproteinase**-2 and **membrane type 1 matrix metalloproteinase** through β1 **integrin** in relation to adhesion to)
IT Signal transduction, biological
(ovarian carcinoma regulation of **matrix metalloproteinase**-2 and **membrane type 1 matrix metalloproteinase** through β1 **integrin**)
IT Cell adhesion
(ovarian carcinoma regulation of **matrix metalloproteinase**-2 and **membrane type 1 matrix metalloproteinase** through β1 **integrin** in relation to)
IT Collagens, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(type I; ovarian carcinoma regulation of **matrix metalloproteinase**-2 and **membrane type 1 matrix metalloproteinase** through β1 **integrin** in relation to adhesion to)
IT **Integrins**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(β1; ovarian carcinoma regulation of **matrix metalloproteinase**-2 and **membrane type 1 matrix metalloproteinase** through β1 **integrin**)
IT 146480-35-5, Gelatinase A 148969-98-6, Pro-gelatinase A
161384-17-4, Membrane type 1 matrix metalloproteinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ovarian carcinoma regulation of **matrix metalloproteinase**-2 and **membrane type 1 matrix metalloproteinase** through β1 **integrin**)
RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
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IT **161384-17-4, Membrane type 1 matrix metalloproteinase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ovarian carcinoma regulation of **matrix metalloproteinase**-2 and **membrane type 1 matrix metalloproteinase** through β1 **integrin**)

RN 161384-17-4 HCAPLUS
CN Proteinase, matrix metallo-, MT-MMP-1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L54 ANSWER 15 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1998:802538** HCAPLUS
DN **130:195628**
ED Entered STN: 23 Dec 1998
TI The interrelationship of α 4 **integrin** and **matrix metalloproteinase**-2 in the pathogenesis of experimental autoimmune encephalomyelitis
AU Graesser, Donnasue; Mahooti, Sepi; Haas, Tara; Davis, Sandra; Clark, Robert B.; Madri, Joseph A.
CS Departments of Pathology and Immunobiology, Yale University School of Medicine, New Haven, CT, 06510, USA
SO Laboratory Investigation (**1998**), 78(11), 1445-1458
CODEN: LAINAW; ISSN: 0023-6837
PB Lippincott Williams & Wilkins
DT Journal
LA English
CC 15-8 (Immunochemistry)
AB Previous studies have suggested that surface expression of **.alpha** .4 **integrin** by autoreactive T-cell **clones** is necessary for the **clones** to induce exptl. autoimmune encephalomyelitis (EAE), a mouse model for human multiple sclerosis. To provide direct evidence for this phenomenon, the authors have transfected **.alpha** .4 **integrin** into C19α 4-LO, a myelin basic protein-reactive T-cell **clone** that does not express . **alpha.**4 **integrin** and does not induce EAE when adoptively transferred into a susceptible mouse strain. Transfection of . **alpha.**4 **integrin** converted this **clone** to an .

alpha.4 **integrin**-expressing **clone** that induced EAE. The authors then examined potential mechanisms by which **.alpha** .4 **integrin** may facilitate the disease process. C19 T-cell **clones** adhered equally to a monolayer of microvascular endothelial cells, regardless of level of α 4 **integrin** expression. However, in contrast to T-cell **clones** that do not express α 4 **integrin**, T-cell **clones** that express α 4 **integrin** (endogenously or by transfection) transmigrated through an endothelial cell layer and subendothelial **matrix** at an enhanced rate and adhered to **recombinant** vascular cell adhesion mol.-1 (rVCAM-1) and the CS1 fragment of fibronectin, and after adhesion to these ligands, a **matrix**-degrading **metalloproteinase** (**MMP**-2) was induced and activated. The **clones** were also shown to constitutively express the membrane-type **matrix** **metalloproteinase** (**MT1-MMP**), an enzyme that activates **MMP**-2. GM 6001 and UK-221, 316, inhibitors of **metalloproteinases**, reduced α 4 **integrin** -mediated transmigration and EAE induction by C19 T-cell **clones.** In addition, the authors studied a second EAE-inducing T-cell **clone** , MM4, which constitutively expresses α 4 **integrin** and **MMP**-2. Engagement of α 4 **integrin** on the MM4 **clone** up-regulated the expression and activation of **MMP**-2, without changing the expression of **MT1-** **MMP.** **MMP** inhibitors also reduced transmigration of and EAE induction by the MM4 T-cell **clone.** These studies demonstrate directly that expression of α 4 **integrin** by autoreactive T-cell **clones** is required for adoptive transfer of EAE in this model. The authors also define a role for α 4 **integrin** in the disease process in mediating the induction and coordinate activation of a **matrix** **metalloproteinase** (**MMP**-2), which facilitates T-cell transmigration.

ST alpha4 **integrin matrix metalloproteinase** T cell autoimmune encephalomyelitis; multiple sclerosis T cell alpha4 **integrin matrix metalloproteinase**

IT Cell adhesion
(T cell; α 4 **integrin** induction and activation of **matrix metalloproteinase**-2 in mediating T-cell endothelial transmigration and pathogenesis of autoimmune encephalomyelitis in mouse)

IT Cell adhesion molecules
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(VCAM-1; α 4 **integrin** induces T-cell adhesion to VCAM-1 in pathogenesis of autoimmune encephalomyelitis in mouse)

IT T cell (lymphocyte)
(adhesion; α 4 **integrin** induction and activation of **matrix metalloproteinase**-2 in mediating T-cell endothelial transmigration and pathogenesis of autoimmune encephalomyelitis in mouse)

IT Encephalomyelitis
(autoimmune; α 4 **integrin** induction and activation of **matrix metalloproteinase**-2 in mediating T-cell endothelial transmigration and pathogenesis of autoimmune encephalomyelitis in mouse)

IT Cell migration
(leukocyte transendothelial; α 4 **integrin** induction and activation of **matrix metalloproteinase** -2 in mediating T-cell endothelial transmigration and pathogenesis of autoimmune encephalomyelitis in mouse)

IT Leukocyte
(transendothelial migration; α 4 **integrin**

induction and activation of **matrix metalloproteinase** -2 in mediating T-cell endothelial transmigration and pathogenesis of autoimmune encephalomyelitis in mouse)

IT Fibronectins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(α 4 **integrin** induces T-cell adhesion to fibronectin in pathogenesis of autoimmune encephalomyelitis in mouse)

IT Disease models
Mouse
(α 4 **integrin** induction and activation of **matrix metalloproteinase**-2 in mediating T-cell endothelial transmigration and pathogenesis of autoimmune encephalomyelitis in mouse)

IT Multiple sclerosis
(α 4 **integrin** induction and activation of **matrix metalloproteinase**-2 in mediating T-cell endothelial transmigration and pathogenesis of autoimmune encephalomyelitis in mouse in relation to)

IT **Integrins**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(α 4; α 4 **integrin** induction and activation of **matrix metalloproteinase**-2 in mediating T-cell endothelial transmigration and pathogenesis of autoimmune encephalomyelitis in mouse)

IT 124861-55-8, TIMP-2 **161384-17-4, MT1-MMP**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(constitutive expression on α 4 **integrin** -expressing T-cells in relation to **matrix metalloproteinase**-2 activation and autoimmune encephalomyelitis pathogenesis in mouse)

IT 146480-35-5, **Matrix metalloproteinase**-2
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(α 4 **integrin** induction and activation of **matrix metalloproteinase**-2 in mediating T-cell endothelial transmigration and pathogenesis of autoimmune encephalomyelitis in mouse)

RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD

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IT **161384-17-4**, **MT1-MMP**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(constitutive expression on α 4 **integrin** -expressing T-cells in relation to **matrix metalloproteinase**-2 activation and autoimmune encephalomyelitis pathogenesis in mouse)
RN 161384-17-4 HCAPLUS
CN Proteinase, matrix metallo-, MT-MMP-1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L54 ANSWER 16 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1998:700543** HCAPLUS
DN **130:50194**
ED Entered STN: 04 Nov 1998
TI The activation of ProMMP-2 (gelatinase A) by HT1080 fibrosarcoma cells is promoted by culture on a fibronectin substrate and is concomitant with an increase in processing of **MT1-MMP** (**MMP-14**) to a 45 kDa form
AU Stanton, Heather; Gavrilovic, Jelena; Atkinson, Susan J.; d'Ortho, Marie-Pia; Yamada, Kenneth M.; Zardi, Luciano; Murphy, Gillian

CS School of Biological Sciences, University of East Anglia, Norwich, NR4 7TJ, UK
SO Journal of Cell Science (**1998**), 111(18), 2789-2798
CODEN: JNCSAI; ISSN: 0021-9533
PB Company of Biologists Ltd.
DT Journal
LA English
CC 13-2 (Mammalian Biochemistry)
AB We have assessed the effect of fibronectin and laminin-1 on the expression of mols. involved in the activation pathway of **MMP**-2, a key **proteinase** in tissue remodeling. HT1080 fibrosarcoma cells cultured on fibronectin were shown to activate endogenous **MMP**-2, to a level comparable with that elicited by treatment with phorbol ester. In contrast, the **MMP**-2 expressed by HT1080 cells cultured on laminin-1 was mainly in the pro- (inactive form). Culture of the cells on peptide fragments of fibronectin derived from the central cell binding domain also promoted **MMP**-2 activation, indicating that signals via fibronectin binding to **integrin** receptors may be involved. HT1080 cells cultured on immobilized antibodies to the α 5 and β1 **integrin subunits** secreted levels of active **MMP**-2 similar to those observed for full length fibronectin, whereas cells cultured on an antibody to the α 6 **integrin subunit** secreted mainly proMMP-2. The data demonstrate that the activation of **MMP**-2 by HT1080 cells is regulated by the nature of the extracellular **matrix**, and that signals via the α 5β1 **integrin** receptor may be involved in the fibronectin induced up-regulation of **MMP**-2 activation. We then assessed the effect of fibronectin on the components of the putative **MT1-MMP**/TIMP-2 "receptor" complex implicated in **MMP**-2 activation. Levels of TIMP-2 protein expressed by HT1080 cells did not vary detectably between cells cultured on fibronectin or laminin-1. However, the expression of **MT1-MMP** protein was up-regulated when the cells were cultured on fibronectin, which could be attributed to an increase in levels of a truncated 45 kDa form. Parallel studies using gelatin zymog. demonstrated that the up-regulation of the production of the 45 kDa band was concomitant with **MMP**-2 activation. Inhibitor studies revealed that the truncation of **MT1-MMP** to a 45 kDa form is **MMP** mediated, although not inhibited by TIMP-1. In vitro, the 45 kDa form could be generated by **cleavage** of membrane-bound native **MT1-MMP** with several **recombinant MMPs**, including both active **MT1-MMP** and **MMP**-2. The implication that either **MMP**-2 or **MT1-MMP** can process **MT1-MMP** to 45 kDa, raises the possibility that truncation of **MT1-MMP** represents a self-regulatory end-point in the activation pathway of **MMP**-2.
ST fibronectin MMP2 **matrix metalloproteinase** activation MT1MMP
IT Laminins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(1; activation of ProMMP-2 by HT1080 fibrosarcoma cells is promoted by culture on fibronectin substrate and concomitant with an increase in processing of **MT1-MMP** to a 45 kDa form)
IT Animal cell line
(HT-1080; activation of ProMMP-2 by HT1080 fibrosarcoma cells is promoted by culture on fibronectin substrate and concomitant with an increase in processing of **MT1-MMP** to a 45 kDa form)
IT Fibronectins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(activation of ProMMP-2 by HT1080 fibrosarcoma cells is promoted by culture on fibronectin substrate and concomitant with an increase in

processing of **MT1-MMP** to a 45 kDa form)

IT **Integrins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(α **5**.beta.1; activation of ProMMP-2 by HT1080 fibrosarcoma cells is promoted by culture on fibronectin substrate and concomitant with an increase in processing of **MT1-MMP** to a 45 kDa form)

IT 124861-55-8, TIMP-2 141907-41-7, **Matrix metalloproteinase** 146480-35-5, Gelatinase A 148969-98-6, ProMMP-2 **161384-17-4**, **MT1-MMP**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(activation of ProMMP-2 by HT1080 fibrosarcoma cells is promoted by culture on fibronectin substrate and concomitant with an increase in processing of **MT1-MMP** to a 45 kDa form)

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IT **161384-17-4**, **MT1-MMP**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(activation of ProMMP-2 by HT1080 fibrosarcoma cells is promoted by culture on fibronectin substrate and concomitant with an increase in processing of **MT1-MMP** to a 45 kDa form)

RN 161384-17-4 HCAPLUS
CN Proteinase, matrix metallo-, MT-MMP-1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L54 ANSWER 17 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1998:552072** HCAPLUS
DN **129:271934**
ED Entered STN: 01 Sep 1998
TI Remodeling of collagen **matrix** by human tumor cells requires activation and cell surface association of **matrix metalloproteinase**-2
AU Deryugina, Elena I.; Bourdon, Mario A.; Reisfeld, Ralph A.; Strongin, Alex
CS La Jolla Institute for Experimental Medicine, La Jolla, CA, 92037, USA
SO Cancer Research (**1998**), 58(16), 3743-3750
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
CC 6-1 (General Biochemistry)
Section cross-reference(s): 14
AB The authors assessed the functional significance of tumor cell-associated **matrix metalloproteinase** (**MMP**)-2 in extracellular **matrix** remodeling compared with that of the soluble enzyme by evaluating the contraction of three-dimensional collagen lattices by human glioma U251.3 and fibrosarcoma HT-1080 cell lines. In this model, the constitutive synthesis and activation of the **MMP**-2 proenzyme were modulated by stable transfections of tumor cells with cDNA encoding membrane type 1-**MMP** (**MT1-MMP**). The efficiency of transfected cells in contracting collagen lattices was shown to be dependent on the **MT1-MMP**-mediated activation of **MMP**-2 accompanied by cell surface association of activated **MMP**-2, on the cell-**matrix** interactions controlled by collagen-specific **integrins**, and on the integrity of actin and microtubule cytoskeletons. Each one of these mechanisms was essential but was not sufficient by itself in accomplishing gel contraction by **MT1-MMP**-transfected cells. Both **MMP**-2 activation and gel contraction by transfected glioma cells were inhibited by tissue inhibitor of **metalloproteinase** (TIMP)-2

and the **recombinant** COOH-terminal domain of **MMP**-2. However, the kinetics and mechanisms of their inhibitory effects were different, because TIMP-2 and the COOH-terminal domain of **MMP**-2 preferentially inhibited the **MT1-MMP**-dependent and autocatalytic steps of **MMP**-2 activation, resp. By contrast, TIMP-1, an efficient inhibitor of soluble **MMP**-2 activity, failed to affect gel contraction. In addition, soluble **MMP**-2 activated by either organomercurials or cells was not able to induce the contraction of collagen lattices when added to transfected cells. Therefore, soluble activated **MMP**-2, sensitive to TIMP-1 inhibition, does not mediate collagen gel contraction by tumor cells, whereas the activity of cell surface-associated **MMP**-2 plays a critical role in remodeling of the extracellular **matrix** in vitro. These mechanisms of functional and spatial regulation of **MMP**-2 may also be applicable to different aspects of tissue reorganization in vivo, including cell migration and invasion, **angiogenesis**, and wound healing.

ST extracellular **matrix** tumor remodeling **matrix** **metalloproteinase**

IT Cell membrane
(**MMP**-2 localization to; cell surfase-associated **MMP**-2 but not soluble enzyme contribute to cell-mediated remodeling of extracellular **matrix**)

IT Extracellular **matrix**
Neoplasm
(cell surfase-associated **MMP**-2 but not soluble enzyme contribute to cell-mediated remodeling of extracellular **matrix**)

IT Collagens, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cell surfase-associated **MMP**-2 but not soluble enzyme contribute to cell-mediated remodeling of extracellular **matrix**)

IT Cytoskeleton
Microtubule
(necessity for actin and microtubule cytoskeleton integrity and **integrins**; cell surfase-associated **MMP**-2 but not soluble enzyme contribute to cell-mediated remodeling of extracellular **matrix**)

IT **Integrins**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(necessity for actin and microtubule cytoskeleton integrity and **integrins**; cell surfase-associated **MMP**-2 but not soluble enzyme contribute to cell-mediated remodeling of extracellular **matrix**)

IT Actins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(necessity for actin and microtubule cytoskeleton integrity and **integrins**; cell surfase-associated **MMP**-2 but not soluble enzyme contribute to cell-mediated remodeling of extracellular **matrix**)

IT **161384-17-4**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(activation by; cell surfase-associated **MMP**-2 but not soluble enzyme contribute to cell-mediated remodeling of extracellular **matrix**)

IT 146480-35-5, **Matrix metalloproteinase**-2
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(cell surfase-associated **MMP**-2 but not soluble enzyme contribute to

cell-mediated remodeling of extracellular **matrix**)
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
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IT **161384-17-4**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(activation by; cell surfase-associated **MMP**-2 but not soluble enzyme contribute to cell-mediated remodeling of extracellular **matrix**)
RN 161384-17-4 HCAPLUS
CN Proteinase, matrix metallo-, MT-MMP-1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L54 ANSWER 18 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1997:725187** HCAPLUS
DN **128:32873**
ED Entered STN: 17 Nov 1997
TI **Matrix metalloproteinase**-2 activation modulates glioma

cell migration
AU Deryugina, Elena I.; Bourdon, Mario A.; Luo, Guang-Xiang; Reisfeld, Ralph A.; Strongin, Alex
CS La Jolla Institute for Experimental Medicine, La Jolla, CA, USA
SO Journal of Cell Science (**1997**), 110(19), 2473-2482
CODEN: JNCSAI; ISSN: 0021-9533
PB Company of Biologists
DT Journal
LA English
CC 13-6 (Mammalian Biochemistry)
AB Stable transfection of U251.3 glioma cells with cDNA encoding **MT-MMP**-1 resulted in increased cell surface expression of **MT-MMP**-1 and TIMP-2, constitutive activation of **MMP**-2 proenzyme and increased collagen degradation In tumor spheroid outgrowth assays, cell migration of **MT-MMP**-1 transfectants relative to control was enhanced on collagen and decreased on vitronectin and fibronectin. These effects were reversed by TIMP-2 and were not associated with any substantial changes in cell adhesion. Binding of U251.3 cells to the C-terminal domain of **MMP**-2 was specifically inhibited by anti-α vβ3 **integrin** blocking antibody indicating that **MMP**-2 interacts with . **alpha.**vβ3 through the enzyme's C-terminal portion at or near the **integrin**'s **matrix** adhesion sites. We propose that these mechanisms could govern directed **matrix** degradation in the tumor cells' microenvironment by sequestration of active **MMP**-2 on the cell surface. Our data suggest that activation of **MMP**-2 and its proteolytic activity localized to the cell surface could differentially modulate tumor cell migration in response to particular **matrix** proteins by altering both composition of the extracellular **matrix** and expression of adhesion receptors on the cell surface.
ST **matrix metalloproteinase** 2 activation cell migration; MMP2 MTMMP1 extracellular **matrix integrin** glioma
IT Decomposition
(**MT-MMP**-1 transfected glioma cells activate **MMP**-2 proenzyme and increase collagen degrdn)
IT Extracellular **matrix**
(activation of **MMP**-2 proenzyme and accumulation of activated **MMP**-2 modulate glioma cell migration in response to extra cellular **matrix** components)
IT Tenascins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(activation of **MMP**-2 proenzyme and accumulation of activated **MMP**-2 modulate glioma cell migration in response to extra cellular **matrix** components)
IT Fibronectins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(activation of **MMP**-2 proenzyme and accumulation of activated **MMP**-2 modulate glioma cell migration in response to extra cellular **matrix** components)
IT Vitronectin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(activation of **MMP**-2 proenzyme and accumulation of activated **MMP**-2 modulate glioma cell migration in response to extra cellular **matrix** components)
IT Cell adhesion
(binding of glioma cells to C-terminal domain of **MMP**-2 in relation to **integrin** α Vβ3)
IT Neuroglia
(glioma; **matrix metalloproteinase**-2 activation modulates glioma cell migration)

IT Cell migration
(**matrix metalloproteinase**-2 activation modulates glioma cell migration)
IT Collagens, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(type I; **MT-MMP**-1 transfected glioma cells activate **MMP**-2 proenzyme and increase collagen degrdn)
IT **Integrins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(α **v**.beta.3; cell surface expression of **integrin** α **V**.beta.3 in **MT-MMP**-1 transfected glioma cells)
IT 124861-55-8, TIMP-2 **161384-17-4**, **MT MMP**-1
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**MT MMP**-1/TIMP-2 regulated **matrix metalloproteinase**-2 activation affects glioma cell migration)
IT 146480-35-5, **Matrix metalloproteinase**-2
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**matrix metalloproteinase**-2 activation modulates glioma cell migration)
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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(2) Aimes, R; J Biol Chem 1995, V270, P5872 HCAPLUS
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IT **161384-17-4**, **MT MMP**-1
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**MT MMP**-1/TIMP-2 regulated **matrix metalloproteinase**-2 activation affects glioma cell migration)
RN 161384-17-4 HCAPLUS
CN Proteinase, matrix metallo-, MT-MMP-1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> => fil biosis
FILE 'BIOSIS' ENTERED AT 14:04:31 ON 08 JUN 2004

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 2 June 2004 (20040602/ED)

FILE RELOADED: 19 October 2003.

=> d l64 all tot

L64 ANSWER 1 OF 2 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2002:260892 BIOSIS
DN PREV200200260892
TI Expression of **integrins** and MMPs during alkaline-burn-induced corneal angiogenesis.
AU **Zhang, Heying**; Li, Chen; **Baciu, Peter C.** [Reprint author]
CS Allergan, Inc., 2525 Dupont Drive, Irvine, CA, 92612, USA
baciu_peter@allergan.com
SO **IOVS**, (April, 2002) Vol. 43, No. 4, pp. 955-962. print.
DT Article
LA English
ED Entered STN: 24 Apr 2002
Last Updated on STN: 24 Apr 2002
AB PURPOSE: To determine in a corneal alkaline burn model of angiogenesis whether the expression of **integrins** and MMPs is consistent with a VEGF-induced angiogenic response. METHODS: Neovascularization in female Sprague-Dawley rats was induced by alkaline cauterization of the central cornea. RT-PCR for **integrins** alpha1, alpha2, beta3, and beta5; the endothelial marker CD31; and **metalloproteinases MMP**-2 and **MT1-MMP** was performed on naive corneas and on cauterized corneas 72 and 288 hours after cautery. Analyses of protein and MMP expression were conducted on naive corneas and on cauterized corneas 24, 72, 120, and 168 hours after cautery by immunofluorescence microscopy and gelatin zymography. RESULTS: RT-PCR indicated a correlation between the induced angiogenic response and the expression of alpha1 and beta3 **integrin** subunits and **MT1-MMP**. Immunohistochemical analysis indicated that alpha1, alpha2, alpha5, and

beta5 **integrins** and **MMP**-2 and **MT1**-**MMP** were expressed on the newly developing vasculature. The beta3 **integrin** was preferentially expressed on platelets. CONCLUSIONS: **Integrin** expression during neovascularization of rat corneas in response to alkaline injury correlates with an angiogenic response that uses the VEGF/alphavbeta5 pathway. **MMP**-2 and **MT1**-**MMP**, but not **MMP**-9, are expressed in a pattern consistent with their involvement in the angiogenic response.

CC Biochemistry studies - General 10060
Enzymes - General and comparative studies: coenzymes 10802
Sense organs - Physiology and biochemistry 20004

IT Major Concepts
Biochemistry and Molecular Biophysics; Sense Organs (Sensory Reception)

IT Parts, Structures, & Systems of Organisms
cornea: sensory system

IT Chemicals & Biochemicals
CD31; alkaline; alpha-1 **integrin**; alpha-2 **integrin**; beta-3 **integrin**; beta-5 **integrin**; matrix metalloproteinases

IT Miscellaneous Descriptors
corneal angiogenesis: alkaline-burn-induced; neovascularization

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
Sprague-Dawley rat: animal model, female
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

RN 141907-41-7 (matrix metalloproteinases)

L64 ANSWER 2 OF 2 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2001:287268 BIOSIS
DN PREV200100287268
TI Analysis of **integrin** expression during corneal neovascularization.
AU **Baciu, P. C.** [Reprint author]; **Zhang, H.** [Reprint author]
CS Dept Biology, Allergan Inc., Irvine, CA, 92612, USA
SO **IOVS**, (March 15, 2001) Vol. 42, No. 4, pp. S94. print.
Meeting Info.: Annual Meeting of the Association for Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. April 29-May 04, 2001.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 13 Jun 2001
Last Updated on STN: 19 Feb 2002
CC Cardiovascular system - Physiology and biochemistry 14504
General biology - Symposia, transactions and proceedings 00520
Cytology - Animal 02506
Biochemistry studies - Proteins, peptides and amino acids 10064
Enzymes - General and comparative studies: coenzymes 10802
Endocrine - General 17002
Sense organs - Physiology and biochemistry 20004
Sense organs - Pathology 20006

IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Sense Organs (Sensory Reception); Cardiovascular System (Transport and Circulation)

IT Parts, Structures, & Systems of Organisms
cornea: sensory system, central area; corneal epithelial cell: sensory system; corneal vasculature: circulatory system, sensory system, development; inflammatory cell, invasion

IT Diseases
corneal alkaline burn: eye disease, injury
IT Chemicals & Biochemicals
CD31: endothelial marker, expression; **MT1**-matrix **metalloproteinase**: expression, protein levels; VEGF [vascular endothelial growth factor]; alpha 1 **integrin**: expression, protein levels; alpha 2 **integrin**: expression, protein levels; beta 3 **integrin**: expression, protein levels; beta 5 **integrin**: expression, protein levels; collagen type IV: extracellular matrix protein; fibronectin: extracellular matrix protein; laminin: extracellular matrix protein; matrix metalloproteinase-2: expression, **integrin**; matrix metalloproteinase-9: expression, **integrin**
IT Miscellaneous Descriptors
corneal neovascularization: alkali burn-induced, vascular endothelial growth factor-induced; Meeting Abstract
ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
Sprague-Dawley rat: animal model, female
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
RN 146480-35-5 (matrix metalloproteinase-2)
146480-36-6 (matrix metalloproteinase-9)
127464-60-2 (VASCULAR ENDOTHELIAL GROWTH FACTOR)

=> => fil wpix
FILE 'WPIX' ENTERED AT 14:18:54 ON 08 JUN 2004

FILE LAST UPDATED: 3 JUN 2004 <20040603/UP>
MOST RECENT DERWENT UPDATE: 200435 <200435/DW>
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http://www.stn-international.de/archive/stnews/news0104.pdf <<<

>>> SINCE THE FILE HAD NOT BEEN UPDATED BETWEEN APRIL 12-16
THERE WAS NO WEEKLY SDI RUN <<<

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L74 ANSWER 1 OF 4 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2004-316460 [29] WPIX
DNC C2004-120061
TI New peptides that regulate the degradation of type II collagen, useful for diagnosing and treating for e.g. osteoarthritis, rheumatoid arthritis, post-traumatic osteoarthritis, idiopathic osteoarthritis or eye diseases.
DC B04 D16
IN POOLE, A R
PA (SHRI-N) SHRINERS HOSPITALS FOR CHILDREN
CYC 106
PI WO 2004031206 A2 20040415 (200429)* EN 74 C07K000-00
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
ADT WO 2004031206 A2 WO 2003-US30744 20030930
PRAI US 2002-414332P 20020930
IC ICM C07K000-00
AB WO2004031206 A UPAB: 20040505
NOVELTY - An isolated or purified peptide comprising a fully defined amino acid sequence of CB12, CB12-I, CB12-II, CB12-III, CB12-IV, Pro6, Pro15, Pro18 or Pro21, or its fragment, conservatively substituted variant, mimetic, inhibitor or homologue, is new. The peptide alters the rate of degradation of type II collagen or the rate of chondrocyte hypertrophy.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a peptide dimer or trimer consisting of 2 or 3 peptides, respectively, where each peptide is selected from the peptides cited above;

(2) a pharmaceutical composition comprising a pharmaceutical carrier and at least one of the peptide inhibitors cited above;

(3) a method of regulating collagen turnover;

(4) a method of identifying a peptide mimetic of a peptide fragment of collagen capable of decreasing the degradation of the collagen in a biological sample;

(5) an isolated or purified antibody that specifically binds to an epitope of the peptide or its antigenic fragment;

(6) a method of diagnosing a disease selected from osteoarthritis, rheumatoid arthritis, post-traumatic osteoarthritis, idiopathic osteoarthritis and eye disease;

(7) a method of inhibiting chondrocyte hypertrophy in a subject; and

(8) a method of screening for a compound capable of inhibiting collagen breakdown.

ACTIVITY - Osteopathic; Antiarthritic; Antirheumatic; Ophthalmological. No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The pharmaceutical composition is useful for reducing collagen matrix turnover in mammals, particularly humans, or for reducing degradation of one or more collagen proteins. The antibody is used to inhibit the activity of the peptide, to identify inhibitors of the generation of the peptide, or to identify a subject at risk for rapid or slow progression of a disease responding to therapy designed to arrest cartilage degradation or at risk for a disease by showing of early

pre-clinical changes prior to clinical presentation of the disease, where the disease is selected from osteoarthritis, rheumatoid arthritis, post-traumatic osteoarthritis, idiopathic osteoarthritis and eye disease. In addition, the antibody is used to detect the release of type II collagen degradation products in body fluids, e.g. tissue extracts, serum, synovial fluid or urine (all claimed). The composition and methods may be used for diagnosing and treating such diseases.
Dwg.0/12

FS CPI

FA AB; DCN

MC CPI: B04-B04B1; B04-B04D4; B04-C01A; B04-G01; B04-N02A; **B12-K04A** ; **B12-K04E**; B14-C09A; B14-C09B; B14-L06; B14-N01; B14-N03; B14-S03; D05-C11; **D05-H09**; D05-H11; D05-H17A6

TECH UPTX: 20040505
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Peptide: The peptide or its fragment is further modified by hydroxylation. The asterisk in the peptide sequence denotes sites of hydroxylation. The peptide or its fragment is hydroxylated at one or more of the proline or lysine residues of the peptide. It is hydroxylated at proline or lysine residues located within the sequence Gly-X-Pro or Gly-X-Lys, where X indicates any amino acid, and where 1-5 acids of the peptide sequence have been replaced using conservative substitutions. The peptide homologue is at least 80% homologous to the peptide. The peptide dimer or trimer is a homodimer or heterodimer, or a homotrimer or heterotrimer.
Preferred Antibody: The antibody is a monoclonal or a polyclonal antibody.
Preferred Method: Regulating collagen turnover comprises administering to a subject an amount of the pharmaceutical composition cited above.
Identifying a peptide mimetic of a peptide fragment of collagen capable of decreasing the degradation of the collagen in a biological sample comprises screening peptide fragments of collagen, and its variants, for the ability of the peptide fragments to bind preferentially to a specific receptor of the naturally produced peptide fragments but has a lesser ability to activate the matrix degradation pathway. The specific receptors are anti-**integrin** receptors. The activation of the matrix degradation pathway induces the expression of genes selected from COLX, **MMP**-9, TGF-B1, IHH, **MMP**-13, CBFA1, SOX 9, bFGF, pTHrP, caspase-3, **MT1-MMP**, IL-1B and **MMP**-I. The biological sample is a biological fluid selected from tissue extracts, synovial fluid, serum and urine. Diagnosing the diseases cited above comprises contacting a sample with the antibody mentioned above.
Inhibiting chondrocyte hypertrophy in a subject comprises administering to the subject a pharmaceutical amount of the above antibody, where the hypertrophy is inhibited. Screening for a compound capable of inhibiting collagen breakdown comprises incubating the test compound in vitro with an extract containing collagen, adding a compound known to increase degradation of collagen, and selecting the compound capable of decreasing the degradation of collagen as compared with the known compound alone.
Preparation: The peptide was prepared using standard isolation or purification techniques.

ABEX UPTX: 20040505
ADMINISTRATION - Administration is parenteral (e.g. intravenous, subcutaneous, intraperitoneal or intramuscular). No dosage given.

EXAMPLE - No relevant example given.

L74 ANSWER 2 OF 4 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2003-058512 [05] WPIX

DNC C2003-015007

TI Screening for agents which inhibit angiogenesis, used for treating cancer, macular degeneration and retinopathies, comprises screening for agents which inhibit activation of **integrin** alpha subunit by **metalloprotease MT1-MMP.**

DC B04 D16

IN BACIU, P C; MANUEL, V M; ZHANG, H
PA (BACI-I) BACIU P C; (MANU-I) MANUEL V M; (ZHAN-I) ZHANG H; (ALLR) ALLERGAN INC
CYC 101
PI WO 2002081627 A2 20021017 (200305)* EN 24 C12N000-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW
US 2003171271 A1 20030911 (200367) G01N033-574 <--
EP 1393075 A2 20040303 (200417) EN G01N033-543 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
AU 2002307096 A1 20021021 (200433) C12N000-00
ADT WO 2002081627 A2 **WO 2002-US10501 20020403**; US 2003171271 A1 **Provisional US 2001-281512P 20010404**, US 2002-115718 20020403; EP 1393075 A2 EP 2002-763922 20020403, **WO 2002-US10501 20020403**; AU 2002307096 A1 AU 2002-307096 20020403
FDT EP 1393075 A2 Based on WO 2002081627; AU 2002307096 A1 Based on WO 2002081627
PRAI **US 2001-281512P 20010404**; US 2002-115718 20020403
IC ICM C12N000-00; **G01N033-543**; **G01N033-574**
ICS A61K038-16; A61K039-00; A61K039-395; **C12Q001-37**; G01N001-30
AB WO 200281627 A UPAB: 20030121
NOVELTY - Screening for agents which inhibit an angiogenic response comprises:
(a) contacting an inactive pro form or convertase-activated form of an **integrin** alpha subunit, **metalloprotease MT1-MMP** and a candidate agent, under conditions which promote increased activation of the **integrin** subunit; and
(b) correlating inhibition of increased activation with ability of the agent to inhibit angiogenesis.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) treating a patient suffering from a pathological condition in which angiogenesis is partially a causative or perpetuating factor, comprising administering an agent capable of inhibiting an increase in activation of an inactive pro form or convertase-activated form of an **integrin** alpha subunit by **MT1-MMP metalloprotease**;
(2) treating a patient suffering from a pathological condition in which angiogenesis is partially a causative or perpetuating factor, comprising administering an agent that specifically inhibits activation of a pro form of **integrin** alpha subunit alpha 3, alpha 4, alpha 5, alpha 5, alpha 7, alpha 8, alpha 9, alpha 2b, alpha E or more preferably alpha V.
ACTIVITY - Cytostatic; Ophthalmological; Circulatory.
MECHANISM OF ACTION - Antiangiogenic; Activation of a pro form of an **integrin** alpha subunit inhibitor; **MT1-MMP metalloprotease** inhibitor. No biological data is given.
USE - The method is used to screen for agents which inhibit an angiogenic response, and the agents are used in the treatment of associated diseases (claimed) including cancer, macular degeneration and retinopathies (disclosed).
Dwg.0/9
FS CPI
FA AB; DCN
MC CPI: B04-E12; B04-F0100E; **B04-H21**; **B04-H2100E**; B04-L05C; B04-L05C0E; B11-C08D1; B11-C08D2; **B12-K04E**; **B14-D07C**; B14-F02; B14-F02F2; B14-H01; B14-N03;

D05-H09

TECH UPTX: 20030121

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: Correlation is accomplished by observing a difference in migration of the activated form versus the inactive form in electrophoresis or chromatography. Alternatively correlation is achieved using a reporter gene and detection of the presence or absence of reporter gene product indicates inhibition of an increase in alpha subunit activation. Preferably the MMT1-MMP and pro form of the **integrin** alpha subunit are recombinantly expressed within the same cell and the agent is contacted within the cell. Activation of the alpha subunit is accomplished by cleavage of the pro form or a change in glycosylation.

ABEX UPTX: 20030121

ADMINISTRATION - Administration is by injection directly into a tumor or joint, by intraocular implant, or by direct injection into the eye. No specific dosage is given.

EXAMPLE - None given.

L74 ANSWER 3 OF 4 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-171995 [22] WPIX
DNC C2002-053302
TI Identifying alpha v-beta 3 **integrin** inhibitor or enhancer, comprises contacting superactivated alpha v-beta 3 **integrin** with one or more molecules and determining reduced or enhanced **integrin** activity.
DC B04 D16
IN DERYUGINA, E I; STRONGIN, A Y
PA (DERY-I) DERYUGINA E I; (STRO-I) STRONGIN A Y; (BURN-N) BURNHAM INST
CYC 96
PI WO 2002008280 A2 20020131 (200222)* EN 84 C07K014-47
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
US 2002025510 A1 20020228 (200222) C12Q001-00 <--
AU 2001082977 A 20020205 (200236) C07K014-47
ADT WO 2002008280 A2 WO 2001-US23514 20010726; US 2002025510 A1 Provisional US 2000-220706P 20000726, US 2001-916658 20010726; AU 2001082977 A AU 2001-82977 20010726
FDT AU 2001082977 A Based on WO 2002008280
PRAI US 2000-220706P 20000726; US 2001-916658 20010726
IC ICM C07K014-47; **C12Q001-00**
ICS C12N009-64; **C12Q001-68**
AB WO 200208280 A UPAB: 20020409

NOVELTY - Identifying an inhibitor or enhancer of alpha v beta 3 activity comprising contacting superactivated alpha v beta 3 **integrin** with one or more molecules, assaying alpha v beta 3 activity, where reduced or enhanced alpha v beta 3 activity identifies an alpha v beta 3 inhibitor and enhancer, respectively, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a superactivated beta 3 variant, comprising substantially the amino acid sequence of a beta 3 subunit with a threonine analog at position 69 and a glutamine analog at the position 70, where when expressed together with an alpha v subunit, the beta 3 variant forms superactivated alpha v beta 3 **integrin** in the absence of membrane type-1 (**MT1**)-matrix **metalloproteinase** (**MMP**).

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - alpha v- beta 3 **integrin** antagonist; alpha v- beta 3 **integrin** agonist. Experimental protocols were described but no results were given.

USE - The method is useful for identifying alpha v beta 3 inhibitors or enhancers which can be used in molecular medicine, anti-cancer and tissue regeneration therapeutics.
Dwg.0/13

FS CPI
FA AB; DCN
MC CPI: B04-C01G; B04-F02A; B04-G01; B04-N02A; B04-N06; B11-C08E; **B12-K04A**; **B12-K04E**; B14-H01; **D05-H09**; D05-H11; D05-H14B2
TECH UPTX: 20020409
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The alpha-v-beta-3 **integrin** activity is either reduced or enhanced. The superactivated alpha-v-beta-3 **integrin** is expressed on a cell, which is a tumor cell or an immortalized cell, preferably an MCF-7 (undefined) breast carcinoma cell. The cell is transfected with a beta-3 encoding nucleic acid molecule and an **MT1-MMP** encoding nucleic acid molecule, where beta-3 has a fully defined sequence of 788 amino acids as given in the specification, and the **MT1-MMP** has a fully defined 582 amino acid sequence as given in the specification. The cell may alternatively be transfected with a nucleic acid molecule encoding a superactivated beta-3 variant having a fully defined 788 amino acid sequence as given in the specification. The alpha-v-beta-3 **integrin** activity is cell adhesion activity selected from a vitronectin-binding activity, a fibronectin-binding activity, or adhesion to a function blocking alpha-v-beta-3-specific antibody.
Preferred Variant: The superactivated beta-3 variant comprises a threonine at position 69 and a glutamine at position 70, and has a fully defined sequence of 788 amino acids as given in the specification.

L74 ANSWER 4 OF 4 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-656962 [75] WPIX
DNC C2001-193302
TI New antibodies useful for treating growth and proliferative disorders involving angiogenesis such as cancer and tumor, comprise antibodies specific to the epitope of dipeptidyl peptidase IV.
DC B04 D16
IN CHEN, W
PA (UYNY) UNIV NEW YORK STATE RES FOUND; (CHEN-I) CHEN W; (UYNY) UNIV NEW YORK STATE
CYC 96
PI WO 2001074299 A2 20011011 (200175)* EN 77 A61K000-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001056975 A 20011015 (200209) A61K000-00
US 2002132979 A1 20020919 (200264) C07K001-00
US 6573096 B1 20030603 (200339) C12N005-00
JP 2004500116 W 20040108 (200410) 116 C12N015-02
EP 1408908 A2 20040421 (200427) EN A61K006-00
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2001074299 A2 WO 2001-US10735 20010330; AU 2001056975 A AU 2001-56975 20010330; US 2002132979 A1 Provisional US 2000-193987P 20000401, CIP of US 2000-541785 20000403, US 2001-823277 20010330; US 6573096 B1 Provisional US 2000-193987P 20000401, US 2000-541785 20000403; JP 2004500116 W JP 2001-572045 20010330, WO 2001-US10735 20010330; EP 1408908 A2 EP 2001-930438 20010330, WO 2001-US10735 20010330
FDT AU 2001056975 A Based on WO 2001074299; JP 2004500116 W Based on WO 2001074299; EP 1408908 A2 Based on WO 2001074299

PRAI US 2000-541785 20000403; US 2000-193987P 20000401;
US 2001-823277 20010330
IC ICM A61K000-00; A61K006-00; C07K001-00; C12N005-00; C12N015-02
ICS A61K039-395; A61K045-00; A61P003-10; A61P009-00; A61P009-10; A61P009-14; A61P017-02; A61P035-04; A61P043-00; C07K014-00; C07K016-40; C07K017-00; C07K019-00; C12N005-10
AB WO 200174299 A UPAB: 20021031
NOVELTY - A monospecific antibody (I) which specifically binds an epitope of a mammalian serine integral membrane protease, dipeptidyl peptidase IV (DPPIV) (also known as CD26), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a bispecific antibody (II) with binding specificity for a first epitope and a second epitope, where the first epitope is the epitope bound by (I);

(2) an immunoconjugate (III) comprising (I) or (II) joined to a therapeutic agent;

(3) a pharmaceutical composition (IV) for inhibiting angiogenesis comprising (I), (II) or (III) and a pharmaceutically acceptable carrier;

(4) a continuous cell line (V) producing (I); and

(5) stimulating (M1) angiogenesis in a mammal suffering from disease or disorder that may be remedied by an increased blood supply, comprising administering DPPIV modulator, where the blood supply to the affected tissue is increased.

ACTIVITY - Antitumor; Cytostatic; Cardiant; Antidiabetic; Antiulcer; Ophthalmological; Vulnerary. Human breast carcinoma cell line MDA-MB-436 (seprase+DPPIV) and human malignant melanoma cell line LOX (seprase+DPPIV-) were transformed with a retrovirus vector for lacZ tag as described Kern et al., 1994 and 0.5 multiply 106 of these cells were subcutaneously injected into 6-8 week-old female athymic mice. Antibodies or inhibitors were subcutaneously co-inoculated orthotopically with human cancer cells (seprase+DPPIV+ and seprase+DPPIV-), followed by intravenous injection into the tail vein with 250 mu g of the mAb E19, E26 or E3 (anti-DPPIV). Mice were maintained for 2-3 months or until primary tumor reaching 2 cm in diameter, after which the primary tumor and selected organs (lung and liver) were assayed for beta -galactosidase activity. The morphological examination of the established tumors and lung metastases revealed that invasion and metastasis of human cancer cells into mouse tissue had occurred.

MECHANISM OF ACTION - Angiogenesis inhibitor; DPPIV modulator (stimulator) (claimed); seprase-DPPIV antagonist. No biological data was provided.

USE - (I), (II), (III) or (IV) is useful for treating a patient suffering from a growth or proliferative disorder involving angiogenesis, preferably in combination with chemotherapy regimen (claimed). (I) is useful for inhibiting (M2) cancer invasion and angiogenesis in a solid tumor which is metastasized in a patient preferably human where cells of normal tissues do not express levels of DPPIV-seprase complex detected by immunohistochemistry. The method comprises administering a composition comprising (I) to the patient where DPPIV-seprase complex expressed on surface of vascular endothelial cells and invading cancer cells involved in the cancer invasion and angiogenesis, is contacted by (I) which inhibits binding of collagen to the complex, resulting in inhibition of cancer invasion and limiting the blood supply to the tissue of the solid tumor. The method is conducted preferably in conjugation with chemotherapy or with administration of a cytotoxin conjugate (claimed). (M1) is useful for stimulating angiogenesis in a mammal suffering from disease or disorder such as cardiovascular disease, a diabetic ulcer, retinopathy or a non-healing wound, that may be remedied by an increased blood supply (claimed).

Dwg.0/9
FS CPI
FA AB; DCN

MC CPI: B04-F05; B04-G03; B04-G21; B04-G22; B04-L01; B04-L05C; B14-E08; B14-F01; B14-F02; B14-H01; B14-N03; B14-N17B; B14-S04; D05-C03C; D05-H11A; D05-H14B2; D05-H17C1

TECH UPTX: 20011220

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Antibody: (I) is preferably monoclonal or polyclonal. (I) preferably inhibits angiogenesis, where (I) is an antibody or antibody binding fragment that specifically binds to epitope bound by either of anti-DPPIV antibodies E19 or E26, where antigen binding fragment is from F(ab')2, F(ab') and Fv. The mammalian DPPIV is preferably human DPPIV. (I) is preferably a chimeric antibody which is humanized. The second epitope of (II) is an epitope of seprase, **MT1-MMP**, **MMP**-2 or an alpha(3)beta(1)-**integrin.** Preferred Immunoconjugate: (I) comprised in (III) is preferably monoclonal single chain antibody which includes antibody E19 and E26, and therefore (III) is specific to epitope bound by the antibodies. The therapeutic agent is an anti-tumor drug, a cytotoxin, a radioactive agent, a photosensitizer, a second antibody or an enzyme. Preferred Cell Line: In (V), (I) specifically binds to the epitope recognized by monoclonal antibody E3 or F4, which is E19 or E26.

ABEX UPTX: 20011220

WIDER DISCLOSURE - Disclosed as new are the following:
(A) a membrane protease complex, consisting of two homodimers of seprase and DPPIV, initially obtained from human placental capillary endothelial membranes; and
(B) inhibiting capillary sprouting in human cancer.

SPECIFIC ANTIBODIES - Monoclonal antibody of DPPIV is an IgG.2a (claimed).

SPECIFIC HYBRIDOMAS - (V) is E19 hybridoma or E26 hybridoma (claimed).

ADMINISTRATION - Administration of (I) in (M2) is through intravenous, transdermal, intramuscular, oral routes. Dosage of in (M2) is 0.1-300 mg/kg (claimed).

EXAMPLE - The seprase-DPPIV complex had been isolated from human placenta, and antibodies were produced as described Pineiro-Sanchez et al., 1997. The monoclonal antibodies E26, E19, E3 and F4 reacted with DPPIV of the seprase-DPPIV complex, and are not immunoreactive with the seprase subunit or with serine integral membrane proteinases (SIMPs). The antibodies produced were further characterized and were found to have following characteristics: (i) the antibodies specifically bind to the invadopodia of invasive cells grown in collagen or on fibronectin films. (ii) the antibodies antibody fragments fail to react with non-invasive human carcinoma cells grown in collagen or on fibronectin films. (iii) the antibodies antibody fragments bind weakly to differentiated human endothelial cells in collagen or matrix gels and more strongly to sprouting human endothelial cells in collagen or matrix cells, (iv) the antibodies antibody fragments bind weakly with connective tissue cells and more strongly with these induced by wounding, (v) the antibodies antibody fragments block the interaction of collagen matrix with reactive human cells and inhibit the collagen degradation by such cells and (vi) the antibodies or antibody fragments react readily with the catalytic or substrate binding domains of DPPIV and of the seprase-DPPIV complex.

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(FILE 'HOME' ENTERED AT 13:18:39 ON 08 JUN 2004)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 13:19:06 ON 08 JUN 2004
L1 772 S (MMP OR ?METALLOPROTEINASE? OR ?METALLOPROTEASE?)(S)(MT1 OR M
L2 551 S ?METALLO?(S)(?PROTEINASE? OR ?PROTEASE?)(S)(MT1 OR MT 1)

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L3          772 S L1,L2

     FILE 'REGISTRY' ENTERED AT 13:20:12 ON 08 JUN 2004
L4            1 S 161384-17-4

     FILE 'HCAPLUS' ENTERED AT 13:20:34 ON 08 JUN 2004
L5          951 S L4
L6          997 S MT MMP1 OR MT1 MMP OR MMP 14 OR MATRIX()(METALLOPROTEASE OR M
L7          313 S MEMBRANE TYPE 1 MATRIX ()(METALLOPROTEASE OR METALLOPROTEINAS
L8          103 S MEMBRANE TYPE MATRIX ()(METALLOPROTEASE OR METALLOPROTEINASE)
L9         1129 S L3,L5-L8
L10          63 S MATRIX (L) METALLO (L) (PROTEINASE OR PROTEASE) (L) (MT1 OR M
L11        1134 S L9,L10
L12         104 S L11 AND INTEGRIN
                E INTEGRIN/CT
L13        1784 S E47
L14        2446 S E59
L15          44 S L11 AND L13,L14
L16         104 S L12,L15
                E INTEGRINS/CT
                E E3+AL
                E E3+ALL
L17           0 S L11 AND E7,E6,
L18          94 S L11 AND E6+NT,PFT
L19         106 S L16,L18
L20          12 S L19 AND SCREEN?
                E DRUG SCREENING/CT
L21           7 S E3+OLD,NT,PFT AND L19
L22           0 S E4,E5 AND L19
                E E3+ALL
L23           0 S E12+OLD,NT,PFT AND L19
L24           0 S E14+OLD,NT,PFT AND L19
                E SCREENING/CW
L25           7 S E3 AND L19
L26          12 S L20,L21,L25
L27          17 S L19 AND ?ANGIOGEN?
L28           4 S L26 AND L27
                E ANGIOGENESIS/CT
L29          13 S E3+OLD,NT,PFT AND L19
                E E3+ALL
L30           6 S E12+OLD,NT,PFT AND L19
                E E1+ALL
                E E11+ALL
L31           3 S E4 AND L19
L32          21 S L27,L29-L31
L33           6 S L26 AND L32
L34           6 S L28,L33
                SEL DN AN 3 4
L35           2 S L34 AND E1-E6
L36          21 S L20-L32 NOT L34
L37          56 S L19 AND (PD<=20010404 OR PRD<=20010404 OR AD<=20010404)
                E BACIU P/AU
L38           3 S E4-E8 AND L19
                E ZHANG H/AU
L39           0 S E3-E27 AND L19
                E ZHANG HEY/AU
L40           2 S E6 AND L19
                E MANUEL V/AU
L41           1 S E8 AND L19
                E ALLERGAN/PA,CS
L42           2 S E3,E4 AND L19
L43           1 S US20030171271/PN OR (WO2002-US10501 OR US2001-281512#)/AP,PRN
L44           3 S L38-L43
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L45            4 S L35,L44
L46           54 S L37 NOT L45
L47           47 S L46 AND L5
L48            7 S L46 NOT L47
                 SEL DN AN L47 2 13 18 20 21 23 24 30 32 34 37 39 41 43 44 45 47
L49           17 S E1-E51 AND L47
L50           21 S L45,L49 AND L1-L3,L5-L49
L51           21 S L50 AND (?CLON? OR ?RECOMBIN? OR ?CHIMER? OR ?CLEAV? OR PROFO
L52           21 S L51 AND (?PROTEASE? OR ?PROTEINASE? OR ?METALLO? OR MATRIX OR
L53            3 S L52 AND L38-L44
L54           18 S L52 NOT L53

     FILE 'REGISTRY' ENTERED AT 13:59:22 ON 08 JUN 2004

     FILE 'HCAPLUS' ENTERED AT 13:59:32 ON 08 JUN 2004

     FILE 'BIOSIS' ENTERED AT 14:00:41 ON 08 JUN 2004
                 E BACIU P/AU
L55           27 S E3-E7
                 E ZHANG H/AU
L56         1864 S E3-E27
                 E ZHANG HE/AU
L57           38 S E3
L58            4 S E57
                 E MANUEL V/AU
L59         1933 S L55-L***
L60           16 S L59 AND INTEGRIN
L61            4 S L59 AND L11
L62            2 S L61 AND IOVS?/SO
L63            2 S L60 AND L62
L64           12 S L60 NOT L61,L62

     FILE 'BIOSIS' ENTERED AT 14:04:31 ON 08 JUN 2004

     FILE 'WPIX' ENTERED AT 14:05:03 ON 08 JUN 2004
L65           79 S L1/BIX OR L2/BIX OR L6/BIX OR L7/BIX OR L8/BIX OR L10/BIX
L66         1466 S (B04-H21? OR C04-H21?)/MC OR INTEGRIN?/BIX
L67            6 S L65 AND L66
L68            1 S L67 AND G01N033/IC,ICM,ICS,ICA,ICI
L69            2 S L67 AND C12Q/IC,ICM,ICS,ICA,ICI
L70            1 S L67 AND (B14-D07C? OR C14-D07C? OR B12-G01B3 OR C12-G01B3)/MC
L71            5 S L67 AND (B12-K04? OR C12-K04? OR D05-H09)/MC
L72            1 S L43
L73            6 S L67-L72
                 SEL DN AN 2 3
L74            4 S L73 NOT E1-E5

     FILE 'WPIX' ENTERED AT 14:18:54 ON 08 JUN 2004

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